

**Non-invasive prenatal
testing: ethical issues**

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The terms of reference of the Council are:

- to identify and define ethical questions raised by recent developments in biological and medical research that concern, or are likely to concern, the public interest;
- to make arrangements for the independent examination of such questions with appropriate involvement of relevant stakeholders;
- to inform and engage in policy and media debates about those ethical questions and provide informed comment on emerging issues related to or derived from the Nuffield Council on Bioethics' published or ongoing work; and
- to make policy recommendations to Government or other relevant bodies and to disseminate its work through published reports, briefings and other appropriate outputs.

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We would like to thank our six external reviewers (listed in the Appendix), who provided comments and criticisms on an early draft of the report over the 2016 Christmas break, and Dr Gareth Thomas, who carried out a review of the literature on decision making on prenatal screening. Their contributions to the content of the report were significant and helpful.

We are grateful to Alison Toop and Sophie Bertaud for the work they carried out for the project while they undertook temporary research placements at the Council in summer 2016.

Finally, the Council would like to thank the members of the Working Group, for their unfailing enthusiasm, their constructive contributions, and their willingness to listen to and engage with views different to their own.

Foreword

As someone with an inherited genetic condition, prenatal screening has shadowed my whole life. I can remember my father talking about it when I was in my teens, and I first published on the topic more than twenty years ago. But with developments in technology such as the identification and analysis of cell free DNA and next generation sequencing, screening now has implications for every one of us. I may know I have an FGFR3 mutation, but now we all realise that each of us has around one hundred mutations in our genome, and might pass on a raised risk of disease to our offspring. Genetic knowledge has advantages, but also generates potential pitfalls.

To ensure that we benefit from this knowledge, we need safeguards. In a society which is built on the liberal ethos of autonomy, we need to ensure that people are making free and fully informed decisions about their future families. This requires health professionals who are supportive, and information provision that is balanced and accurate. This also means learning about the rich and varied lives of disabled people, not just knowing about genetic spelling mistakes. Finally, it means being confident that our society will welcome disabled children, and support them and their families appropriately.

In order to avoid the potential dangers of a genomic future, we also need to operate within parameters. Few people would object to prospective parents being able to find out about genetic conditions like Down syndrome and other trisomies, or achondroplasia, or many other inherited genetic conditions. But when it comes to less significant information, or non-health-related information, then most people become concerned. Above all, if we are to save prospective parents from the anxiety or confusion of genomic knowledge that no one currently can interpret or use for reliable prediction, we need to set limits. In the future, with fuller knowledge, we might be able to make wise decisions about genetic data. For now, we risk confusion, anxiety, discrimination, and parents knowing more about their children than their children may want to know about themselves.

I am delighted to welcome this report, but also feel sad to have come to the end of a journey with a wonderful team of colleagues, bringing skills from genetic medicine, from counselling, from ethics, from psychology, from law and from public health. We were supported by the dedicated and diligent work of Catherine Joynson, Anna Wilkinson and the whole Nuffield Council on Bioethics team. I would like to acknowledge and thank them all for going beyond the call of duty. Finally, it is also important to thank and value all the individuals who responded to our survey and consultation, who agreed to be interviewed by members of the Working Group, and particularly to the disabled people who took part in our information gathering work. I hope you feel this report appropriately reflects your hopes and concerns.

Professor Tom Shakespeare
Chair of the Working Group

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Terms of reference

The terms of reference of the Working Group on non-invasive prenatal testing (NIPT) were:

- 1 to consider the ethical, legal and regulatory implications of recent and potential future scientific developments in NIPT, with regard to its use in both NHS and commercial services, including for whole genome/exome sequencing;
- 2 to engage a range of people and organisations in the consideration of these questions;
- 3 to report and disseminate findings and recommendations amongst key decision-makers and other stakeholders.

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Executive summary

1. As society's view of disability has changed, so has our view of screening and testing fetuses for genetic conditions. Whereas once these were fairly uncontroversial practises that aimed to reduce ill-health in society, we now recognise that offering pregnant women choices about whether to have a child with a genetic condition or variation is not straightforward. The ability of pregnant women and couples to make choices about their pregnancies is still highly valued, but we now also recognise that having a disabled child is not necessarily detrimental to one's life, and in fact in many cases enhances life in the way having any child would. The public debate surrounding the development of non-invasive prenatal testing (NIPT) has brought this tension into the spotlight like never before.
2. However, this report, in considering the ethical issues raised by NIPT in particular, does not simply weigh up the value of reproductive choice on the one hand versus the interests of disabled people on the other. NIPT is being used in different healthcare contexts and to test for different genetic conditions and traits, with each kind of use offering both advantages and disadvantages to different parties. These parties include not only pregnant women and disabled people, but also fetuses, the people they might become in the future, healthcare professionals and public institutions such as the NHS. The Working Group that oversaw the project sought to consult widely and listen intently to those who have an interest in the increasing use of NIPT (see Appendix for Method of working). We then came to our own conclusions about how policy makers should navigate the challenges posed by current and potential future uses of this technology. Our aim is not to put up barriers to the application of what is undoubtedly a major breakthrough in prenatal screening and testing. Rather, we have taken the opportunity to consider, at this early stage of its use, how NIPT could change the way we view pregnancy, disability and difference, and what the wider consequences of its increasing use might be.

Chapter 1 – Introduction

3. NIPT is a technique that can be used to test for different genetic conditions and features with varying levels of certainty. It has a number of advantages over current screening and diagnostic testing methods. For example, NIPT is more accurate than some other screening tests, it carries no risk of miscarriage and, in some circumstances, it can provide earlier results than current screening and diagnostic tests.
4. NIPT is an accurate prenatal screening test for Down's, Edwards' and Patau's syndromes. Some false positive results occur however, so an invasive test is required to obtain a definitive diagnosis. NIPT for these conditions has been available to women and couples in the UK through private healthcare providers since 2012, and will be offered as part of the NHS fetal anomaly screening programme from 2018. NIPT can also be used to diagnose other genetic conditions and impairments in fetuses, such as cystic fibrosis, and it can determine the sex of the fetus, a service that is widely available through private providers. NIPT for a wider range of conditions or impairments is likely to be available in the future. Whole genome and exome sequencing using NIPT has already been carried out in a research setting.
5. There is no UK-specific professional guidance on NIPT. NHS service specifications set out how prenatal screening and testing should be delivered, and all healthcare professionals must meet standards of conduct set by their professional regulators. The

UK Medical Devices Regulations 2002, which implement an EU Directive, regulate the manufacture of NIPT kits in the UK. The EU Directive does not apply to the many NIPT tests available to women and couples in the UK where the analysis takes place outside of the EU. The Abortion Act 1967 allows terminations of pregnancies to take place on the 'fetal anomaly' ground. The Equality Act 2010 protects disabled people against discrimination and created the Public Sector Equality Duty in England, Scotland and Wales.

6. We have elected to use the term 'significant medical condition or impairment' in this report to describe what would be grounds for termination under the fetal anomaly ground of the Abortion Act 1967. What constitutes a significant medical condition or impairment is a judgment that depends on several factors, including the likely level of impairment, the available treatment options, and the views of and potential impact on the family and the individual themselves.
7. NIPT raises a broad range of ethical issues, which might be understood in terms of the following values:
 - Choice, autonomy and consent – our ability to make free, informed choices about the medical tests and treatments we undergo is considered to be an important principle in modern healthcare.
 - Avoidance of harm – the Government has a duty to eliminate or reduce harms caused by healthcare interventions such as NIPT that are available through the NHS, or to consumers in the private healthcare sector.
 - Equality, inclusion and fairness – the Government and NHS each have a duty to promote equality and ensure that all people are treated fairly. This involves developing policies that address prejudice, bias and discrimination, and ensuring that public money is spent fairly.

Chapter 2 – NIPT in NHS screening for Down's, Edwards' and Patau's syndromes

8. From 2018, pregnant women who are found to have at least a 1 in 150 chance of their fetus having Down's, Edwards' or Patau's syndrome after having the 'combined' screening test will be offered NIPT as a second stage screening test in the NHS. Research suggests that this will increase prenatal diagnoses, giving more women the opportunity to prepare for a disabled child or have a termination, and will lower the number of invasive diagnostic tests, reducing procedure-related miscarriages.
9. It might be thought unfair or inequitable that only some women will be offered NIPT in the NHS. However, offering NIPT to all pregnant women could lead to a higher number of false positive results and test failures, and therefore more invasive diagnostic procedures.
10. Offering NIPT as a second stage test may lead to a delay in diagnosis for some women, which may be significant to those considering a termination.
11. There are concerns that women and couples will think NIPT is equivalent to a diagnostic test or that it is a 'routine' part of prenatal care. Some healthcare professionals may be focusing on medical problems when imparting information about Down's syndrome, without describing more fully what it can be like to have a child with Down's syndrome. Non-NHS sources of advice, the presentation of disability and prenatal testing in the

media, and the perceived impact of a disabled child on the family may also influence the decisions women and couples make. The provision of accurate, balanced information that supports all screening choices equally, and the need for sufficient time to discuss any concerns are essential requirements for the introduction of NIPT in the NHS.

12. Introducing NIPT in the NHS could lead to an increase in the number of terminations following a diagnosis of Down's, Edwards' or Patau's syndrome. Some believe this amounts to eugenics. If this leads to a significant reduction in the number of people born and living with these syndromes, it is possible that the quality of health and social care they receive and the importance attributed to research into these syndromes will be affected. Making NIPT available in the NHS could be perceived as sending negative and hurtful messages about the value of people with the syndromes being tested for.
13. The introduction of NIPT may lead to changes in demand for related NHS services, such as genetic counselling, invasive diagnostic testing, termination and laboratory services. There are no national standards or guidelines on antenatal care for women who choose to continue their pregnancy after a diagnosis of a fetal anomaly.
14. NIPT for other genetic conditions or impairments could be proposed for inclusion in NHS prenatal screening programmes in the future. Recognising that there may be wider consequences of prenatal screening, beyond those being aimed for, is important for the appraisal of the appropriateness of screening programmes.

Chapter 3 – NIPT for rare genetic conditions in the NHS

15. NIPT can be used to test fetuses for rare *de novo* genetic conditions, such as thanatophoric dysplasia, and certain inherited genetic conditions, such as cystic fibrosis. In some cases, NIPT is diagnostic and removes the need for invasive testing. Pregnant women and couples are usually referred by their obstetrician, midwife or GP to a specialist NHS genetic testing service for this kind of prenatal testing.
16. Decisions about what tests should be offered and to which patients are made on a case-by-case basis by doctors such as clinical geneticists. The UK Genetic Testing Network evaluates the scientific validity and clinical utility of new genetic tests that its member laboratories would like to offer NHS patients. Tests from non-NHS, including non-UK, laboratories also can be requested by the genetics team.
17. Healthcare professionals involved in the delivery of prenatal genetic testing services are appropriately trained, and information is given in a timely and non-directive fashion. Genetic counsellors and nurses are widely recognised as an integral part of the multidisciplinary team.
18. The availability of NIPT for rare genetic conditions in the NHS is still quite limited. As NIPT becomes more widely available and if the number of prenatal diagnoses increase in the future, this might reinforce or amplify negative messages about the societal value placed on people with genetic conditions. Prenatal testing can have benefits for people with genetic conditions by enabling them to make informed choices in pregnancy.
19. NIPT for further genetic conditions or 'panel tests' for several related conditions are likely to be developed for NHS use in the future. NIPT for adult onset conditions or carrier status may also become available. Arguments for not genetically testing a child in order to respect the autonomy and interests of the future adult also apply to not testing a fetus for

adult onset conditions in a continuing pregnancy. Testing a fetus for carrier status generally has no immediate clinical use, and may threaten the autonomy and interests of the future person.

20. Whole genome and exome sequencing of fetuses using NIPT might become available in the future. Revealing information about the fetus that is of unknown or uncertain clinical significance could create unnecessary anxiety and lead more women to have invasive diagnostic procedures. This information would also have limited clinical utility, and may be harmful to the person that the fetus might become if it is stored and analysed later.

Chapter 4 – NIPT in the private sector

21. NIPT is available to women and couples on a private basis through hospitals and clinics in the UK. All of the NIPT tests on the market estimate the chance that a fetus has Down's, Edwards' and Patau's syndromes. Some also test for sex and genetic variations such as sex aneuploidy and microdeletions. For the majority of women, privately sought NIPT offers reassurance at an early stage of pregnancy.
22. Many NIPT tests being carried out by UK hospitals and clinics are sent to the USA or China for analysis, and so fall outside UK and EU laws that regulate medical devices. The healthcare professionals offering NIPT in the UK are, however, obliged by their regulating bodies to ensure patients have given properly informed consent for care or treatment. In addition, providers must ensure their advertising material is not misleading or harmful.
23. Although there are some examples of good practice, there is commonly a lack of good quality information from manufacturers, private hospitals and clinics about the limitations of NIPT and the conditions being tested for. The availability of impartial information and support from independent organisations and the NHS is important.
24. There are concerns that the support offered by private NIPT providers to women with a high chance NIPT result can be inadequate, particularly in direct-to-consumer contexts. Women with these results seek follow-up advice and support, invasive diagnostic testing and termination services in the NHS.
25. There is scant or unreliable information on the accuracy of NIPT when used to test fetuses for sex aneuploidy and microdeletions. Where test performance data are available, false positive rates are often much higher, which could lead to more women seeking unnecessary invasive diagnostic tests and experiencing increased anxiety.
26. The offer of NIPT to determine the sex of the fetus at an early stage of pregnancy may increase the risk of sex selective terminations taking place. This practice is opposed by many who believe it to be sexist and wrong. There is some evidence that sex selective terminations have happened in the UK, and they are known to occur in other countries. It is also known that people who live in countries where prenatal sex determination is illegal travel to countries where it is legal to have such tests.
27. As manufacturers compete with each other for their share of market, it is plausible that the trend of offering NIPT for more conditions and traits will continue. Allowing women and couples to access NIPT for less significant medical conditions or non-medical traits would have limited clinical utility, may lead to selective terminations, and may threaten the autonomy and interests of the future person.
28. The same concerns are raised by the prospect of NIPT for whole genome or exome sequencing of fetuses becoming available in the private sector. In addition, much of the

information generated would be difficult to interpret, potentially causing unnecessary anxiety to pregnant women and couples.

Chapter 5 - Ethical values and NIPT

29. The issues raised by NIPT can be cast within a framework based on the values of choice, autonomy and consent; avoidance of harm; and equality, fairness and inclusion. These values may be promoted or undermined by NIPT in different ways for women and couples, the people that fetuses might become, and disabled people. Perspectives on whether, and to what extent, a fetus also has interests that may be harmed by NIPT depend on views about the moral status of the fetus.

- **Choice, autonomy and consent** – NIPT can enhance reproductive autonomy in different ways, including by enabling women and couples to prepare for a baby with a genetic condition or impairment, or decide to have a termination, potentially at an earlier stage of pregnancy. However, NIPT can undermine autonomy and choice if accurate and balanced information about the test and the conditions being tested for is not available, if women and couples feel that they are expected to make a particular decision, or by posing risks to the personal autonomy of the future people that fetuses might become.
- **Avoidance of harm** – NIPT has the potential to reduce harms to pregnant women and fetuses, such as where it can replace or reduce the need for invasive testing. However, NIPT could lead to anxiety and more invasive procedures where inaccurate or unreliable results are returned. If NIPT leads to a significant decrease in the number of people born and living with genetic conditions or impairments, it could lead to fewer resources being invested in research and health and social care relating to people with genetic conditions, and cause offence and social isolation.
- **Equality, fairness and inclusion** – NIPT has the potential to enhance the ability of women to choose the circumstances of their pregnancy, helping to promote equality for women more generally. However, NIPT may give rise to perceptions that people are ‘to blame’ for having a baby with a disability, may change views about what is considered to be a healthy pregnancy or child, and may make disabled people and their families more vulnerable to stigma, discrimination and abuse.

An ethical approach

30. The tensions that exist between the potential benefits and the risks of NIPT, as well as between the ethical values to which they relate, create challenges for public policy. The Working Group suggests three general principles, that should always be considered together, to guide policy making in relation to NIPT:
- **Principle 1.** The wider societal environment in which NIPT is provided and developed should be considered when developing policy relating to NIPT.
 - **Principle 2.** Pregnant women and couples should have access, where appropriate, to NIPT within an environment that enables them to make autonomous, informed choices.
 - **Principle 3.** Efforts should be made to reduce any risks of significant harms posed by the growing use and development of NIPT.

Chapter 6 - Conclusions and recommendations

31. The Working Group uses its ethical approach as the basis for making a number of recommendations for the ethical provision of NIPT. Many of these apply to any provider of NIPT, be that the NHS or a private company, and could apply to the use of NIPT in any country. Some specific issues are raised by the offer of NIPT as part of an NHS screening programme or other NHS service, and by the offer of NIPT by private healthcare providers in the UK, and some additional recommendations are made in each of these areas.

Overarching conclusions and recommendations

32. Women and couples should be able to access NIPT to enable them to find out whether their fetus has a significant medical condition or impairment that manifests at birth or in childhood. However, NIPT should only be offered if it provides an accurate prediction of whether the fetus has or does not have the condition being tested for. In addition, all providers of NIPT have a responsibility to provide high quality information and support to women and couples about the test and the condition being tested for. The Government should ensure it is meeting its duties to provide disabled people with high quality specialist health and social care, and to tackle the discrimination, exclusion and negative societal attitudes experienced by disabled people.
33. NIPT should not normally be used to test whether a fetus has a less significant medical condition or impairment or an adult onset condition; to find out whether the fetus is the carrier of a gene for any kind of medical condition or impairment; nor to reveal non-medical traits of the fetus, including sex. The use of NIPT for whole genome or exome sequencing of fetuses should not normally be offered outside a research environment.
34. Professional guidance for health and social care professionals on the availability and provision of all types of NIPT in the UK should be developed, and existing guidance on the continuation of pregnancy after diagnosis of a fetal anomaly should be updated and expanded.

NIPT in NHS screening for Down's, Edwards' and Patau's syndromes

35. We support the introduction of NIPT for Down's, Edwards' and Patau's syndromes as a second stage screening test in the NHS. Accurate, balanced and non-directive information for women and couples should be developed and published with the involvement of people with different personal experiences. High quality education and training must be compulsory for all health and social care professionals involved in NHS prenatal screening.
36. The UK National Screening Committee should take better consideration of the particular consequences, some of which will be unintended, of prenatal screening programmes where termination of pregnancy is an option.

NIPT for rare genetic diseases in the NHS

37. The NHS should ensure it has an adequate supply of trained genetic counsellors.
38. The use of whole genome or exome sequencing may be justified in rare cases in this context, such as when it is suspected that a fetus has a significant medical condition or impairment of unknown origin.

NIPT in the private sector

39. The Committee of Advertising Practice should more closely monitor the marketing activities of NIPT manufacturers and private hospitals and clinics to ensure that they are not misleading or harmful. Certification from recognised information quality schemes should be sought by NIPT providers to help women and couples to know that their information has been quality checked.
40. Private hospitals and clinics should only offer NIPT as part of an inclusive package of care that should include, at a minimum, pre- and post-test counselling and follow-up invasive diagnostic testing if required.

Chapter 1

Introduction

Chapter 1 – Introduction

Chapter overview

Non-invasive prenatal testing (NIPT) is a technique that can be used to test for different genetic conditions and features with varying levels of certainty. It has a number of advantages over current screening and diagnostic testing methods. For example, NIPT is more accurate than some other screening tests, it carries no risk of miscarriage and, in some circumstances, it can provide earlier results than current screening and diagnostic tests.

NIPT is an accurate prenatal screening test for Down's, Edwards' and Patau's syndromes. Some false positive results occur, however, so an invasive test is required to obtain a definitive diagnosis. NIPT for these conditions has been available to women and couples in the UK through private healthcare providers since 2012 and will be offered as part of the NHS fetal anomaly screening programme from 2018.

NIPT can also be used to diagnose other genetic conditions and impairments in fetuses, such as cystic fibrosis, and it can determine the sex of the fetus, a service that is widely available through private providers. NIPT for a wider range of conditions or impairments is likely to be available in future. Whole genome and exome sequencing using NIPT has already been carried out in a research setting.

There is no UK-specific professional guidance on NIPT. NHS service specifications set out how prenatal screening and testing should be delivered, and all healthcare professionals must meet standards of conduct set by their professional regulators. The UK Medical Devices Regulations 2002, which implement an EU Directive, regulate the manufacture of NIPT kits in the UK. The Abortion Act 1967 allows terminations of pregnancies to take place on the 'fetal anomaly' ground. The Equality Act 2010 protects disabled people against discrimination and created the Public Sector Equality Duty in England, Scotland and Wales.

We have elected to use the term 'significant medical condition or impairment' in this report to describe what would be grounds for termination under the fetal anomaly ground of the Abortion Act 1967. What constitutes a significant medical condition or impairment is a judgment that depends on several factors, including the likely level of impairment, the available treatment options, and the views of and potential impact on the family and the individual themselves.

NIPT raises a broad range of ethical issues, which might be understood in terms of the following values:

- Choice, autonomy and consent – our ability to make free, informed choices about the medical tests and treatments we undergo is considered to be an important principle in modern healthcare.
- Avoidance of harm – the Government has a duty to eliminate or reduce harms caused by healthcare interventions such as NIPT that are available through the NHS, or to consumers in the private healthcare sector.
- Equality, inclusion and fairness – the Government and NHS each have a duty to promote equality and ensure that all people are treated fairly. This involves developing policies that address prejudice, bias and discrimination, and ensuring that public money is spent fairly.

What is NIPT?

- 1.1 Small amounts of DNA, often referred to as 'cell free DNA' (cfDNA), circulate in everybody's blood. In the late 1990s, it was discovered that cfDNA from the placenta can be detected in the blood of pregnant women.¹ The placenta develops from cells formed during the first stage of pregnancy from the fertilised egg; hence, its genetic makeup is very similar, though not always identical, to that of the developing fetus. The amount of placental cfDNA in the woman's blood increases as the pregnancy progresses, and is cleared from the woman's circulation within hours of birth, so it is specific to the woman's current pregnancy. This discovery opened up the possibility of finding out genetic information about the fetus by means of a maternal blood test. Techniques have been developed that reliably test placental cfDNA from around nine weeks of pregnancy, which is when there is usually enough cfDNA in the woman's blood to get an accurate result. This is called non-invasive prenatal testing (NIPT). 'Non-invasive' refers to the fact that the test can be carried out without inserting a needle into the abdomen or cervix of the pregnant woman to collect cells from the amniotic sac or placenta. 'Prenatal' means before birth or during pregnancy.
- 1.2 NIPT can now be used to test for a range of genetic conditions or traits in the fetus. For some inherited single gene disorders, such as achondroplasia and Apert syndrome,² NIPT provides a definitive diagnosis if the disorder is inherited from the father or arises at conception. For other conditions, such as Down's syndrome, NIPT can be used to estimate the chance that a fetus has the condition or not, and an invasive test is required to provide a diagnosis. The accuracy of the estimation varies for different conditions and with different circumstances, such as whether it is a single or multiple pregnancy, or whether the woman is already known to be at increased chance of having a fetus with the condition. NIPT can also be used to determine the sex of the fetus. It is important, therefore, not to think of NIPT as a single test. It is a technique that can be used to test for different genetic conditions and features with varying levels of certainty.
- 1.3 During this project, the Working Group has considered the implications of the use of all kinds of non-invasive prenatal genetic testing using cfDNA from the placenta within maternal blood, including:
 - to estimate the chance that a fetus has Down's, Edwards' or Patau's syndromes, which is commonly referred to as non-invasive prenatal testing or screening;
 - to get a definite or near definite diagnosis of other specific genetic conditions in some cases (e.g. achondroplasia and Apert syndrome). This is sometimes referred to as non-invasive prenatal diagnosis (NIPD);
 - to determine fetal sex; and
 - to perform whole genome or exome sequencing.
- 1.4 NIPT has features that make it different from other prenatal screening and testing techniques. In summary:

¹ Lo YM, Corbetta N, Chamberlain PF *et al.* (1997) Presence of fetal DNA in maternal plasma and serum *Lancet* **350**: 485-7.

² For more information about these conditions see: www.nhs.uk/conditions/restricted-growth and www.nhs.uk/conditions/craniosynostosis

- **NIPT is more accurate³ than other prenatal screening tests** for Down's, Edwards' and Patau's syndromes, such as the combined test (see Box 1.2, p8 and Box 1.3, p13).
- **Compared to invasive diagnostic tests, NIPT carries no risk of miscarriage.** Diagnostic prenatal tests, such as amniocentesis or chorionic villus sampling (CVS), involve taking a sample from the amniotic fluid or placenta and carry a small risk of miscarriage.⁴ NIPT is diagnostic for some conditions and requires only a maternal blood sample, so it carries no risk of miscarriage (NIPT is not diagnostic for Down's, Edwards' and Patau's syndromes).
- **NIPT can, in principle, provide earlier results than current screening tests.** NIPT usually can be performed at nine to ten weeks of pregnancy, with results being delivered usually within a week of the test. Other screening methods, such as the combined screening test for Down's syndrome, and diagnostic invasive tests, such as CVS, can be carried out from approximately eleven weeks of pregnancy.
- **NIPT requires no specialist clinical skills or equipment in the healthcare setting.** NIPT involves taking a sample of blood from the pregnant woman and sending it to a laboratory for analysis. Combined screening or diagnostic tests require the involvement of sonographers and ultrasound equipment at the clinic where the test is taking place. Diagnostic tests are carried out under the care of fetal medicine clinicians. Specialist skills in the provision of information and support are essential for the delivery of NIPT, however, in the same way as they are for other prenatal screening and testing methods.
- **NIPT is no more uncomfortable physically for the woman than standard blood tests.** Specialised diagnostic testing can be unpleasant or painful for some pregnant women.

Prenatal screening for Down's, Edwards' and Patau's syndromes

Down's, Edwards' and Patau's syndromes

- 1.5 'Aneuploidy' is the term given to an unusual number of chromosomes in all or some of a person's cells. Down's syndrome is caused typically by aneuploidy – specifically, an extra copy of chromosome 21 in each cell. Mosaic Down's syndrome occurs when only some of a person's cells have an extra copy of chromosome 21. Translocation Down's syndrome occurs when the extra copy of chromosome 21 attaches to another chromosome. Down's syndrome currently affects approximately 1 in 1000 (0.1 per cent) of live births worldwide.⁵ Usually, Down's syndrome occurs as a random event in the sperm or egg (a '*de novo*' mutation) and is not inherited. Every fetus has a small chance of having Down's syndrome, and this chance increases with the age of the pregnant woman. For example, a woman who is 20 has an approximately 1 in 1500 (0.067 per cent) chance of giving birth to a baby with Down's syndrome, while a woman who is 40

³ The term accuracy can have various meanings. When referring to accuracy in this report, we include specificity, sensitivity, positive predictive value and negative predictive value. See Box 1.2, p30, for an explanation of these terms.

⁴ See Paragraph 1.10 for a discussion of the evidence on the rates of miscarriage associated with amniocentesis and CVS.

⁵ World Health Organization (2016) *Genes and human disease*, available at: <http://www.who.int/genomics/public/geneticdiseases/en/index1.html>.

has a 1 in 100 (1 per cent) chance.⁶ In England and Wales, the number of babies born with Down's syndrome varied from approximately 580 to 780 between 1989 and 2012.⁷ In Scotland, the number of births varied from 36 to 68 (with an average of 59 births) between 2000 and 2009.⁸ Some studies suggest that approximately 30 per cent of fetuses with Down's syndrome spontaneously miscarry between ten weeks and birth; others suggest that this figure could be much lower.⁹

- 1.6 Before the 1960s, people with Down's syndrome mostly lived in state institutions, but attitudes towards people with the syndrome, and disabled people more generally, have changed markedly over the past 50 years. Advances in medical treatment and changes in Government policy regarding the care, support and education of people with learning disabilities in the UK have led to significant improvements in the life expectancy and quality of life of people with Down's syndrome. People with Down's syndrome have a learning disability that can vary from mild to severe in different people. Most people with Down's syndrome at least start their education in the general system, and some have jobs and can live with a substantial degree of independence. Some health problems are more common in people with Down's syndrome, such as heart conditions, problems with the digestive system, hearing and vision, and Alzheimer's disease later in life. Some of these problems can be treated, and today, someone with Down's syndrome is expected to live to approximately 60 years of age.¹⁰ Some people do not consider Down's syndrome to be a medical condition at all, just a difference.
- 1.7 There is a lack of good recent research evidence on the lived experiences of people with Down's syndrome and their families. Two well-designed British cohort studies in Greater Manchester and Surrey followed samples of approximately 100 families and 54 families with a son or daughter with Down's syndrome, respectively, from shortly after their birth until early adulthood in the 1980s and 1990s. Overall, the families in these studies did not have a higher incidence of psychological distress than matched comparison groups. Both studies found that the factors that influence the wellbeing of the person with Down's syndrome and their family were largely the same as those influencing any child and family. There was a wide range of individual differences between the families and between the children themselves. The majority of the families were harmonious with high levels of cohesion and perceived satisfaction with life and relatively normal levels of stress. Approximately one-third of the families experienced more difficulties. Some of these were associated with the lower mental ability, behavioural problems and physical illness of the child; however, difficulties were also associated with family characteristics including lack of financial resources, lower levels of social support, family illness and ineffective coping strategies.¹¹

⁶ NHS (2017) Down's syndrome, available at: <http://www.nhs.uk/conditions/Downs-syndrome/Pages/Introduction.aspx>.

⁷ Morris JK and Springett A (2014) *The National Down Syndrome Cytogenetic Register for England and Wales: 2013 annual report* available at: http://www.binocar.org/content/annrep2013_FINAL_nologo.pdf.

⁸ NHS Scotland (2010) *Scottish perinatal and infant mortality and morbidity report*, available at: <http://www.isdscotland.org/Health-Topics/Maternity-and-Births/Publications/2012-01-31/2012-01-31-spimmr2010-report.pdf>.

⁹ Savva GM, Morris JK, Mutton DE and Alberman E (2006) Maternal age-specific fetal loss rates in Down syndrome pregnancies *Prenatal diagnosis* **26**: 499-504; Loane M, Morris JK, Addor MC *et al.* (2013) Twenty-year trends in the prevalence of Down syndrome and other trisomies in Europe: impact of maternal age and prenatal screening *European Journal of Human Genetics* **21**: 27-33.

¹⁰ Down's Syndrome Association (2016) About, available at: <http://www.downs-syndrome.org.uk/about/general/>; Public Health England (2016) *Screening tests for you and your baby*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/529950/STFYAYB_May_2016_for_website.pdf

¹¹ Cunningham C (1996) Families of children with Down syndrome *Down Syndrome Research and Practice* **4**: 87-95; Carr J (1995) *Down's syndrome. Children growing up*. (Cambridge: Cambridge University Press).

- 1.8 Edwards' syndrome is also caused by aneuploidy, this time by an extra copy of chromosome 18 (or some extra chromosomal 18 material). Patau's syndrome is caused by an extra copy of chromosome 13 (or some extra chromosomal 13 material). Like Down's syndrome, both conditions are rarely inherited and the vast majority occur *de novo*. There were 532 diagnoses of Edwards' syndrome and 232 diagnoses of Patau's syndrome in England and Wales in 2012.¹² In Scotland, between 2000 and 2009, there were on average 12 babies born with Edwards' syndrome and five babies born with Patau's syndrome each year.¹³ Edwards' syndrome affects approximately 1 in every 1500 pregnancies (0.067 per cent) and Patau's syndrome affects approximately 1 in every 4000 pregnancies (0.025 per cent).¹⁴ The chances of these conditions increase with the age of the pregnant woman. Depending on the time in pregnancy when the diagnosis is made, approximately one-third to two-thirds of fetuses with Edwards' or Patau's syndrome will die before they are born. Approximately 50 per cent of babies born alive with one of these syndromes will die within the first week of birth. However, 20 per cent of babies born alive with either condition survive for 3 months and 10 per cent survive for 12 months or more. Active treatment (e.g. to repair heart defects) can significantly increase life expectancy.¹⁵ Babies with one of these two syndromes will have a severe learning disability and many have cardiac defects. Other problems such as feeding difficulties and cleft lip and palate affect some of these babies. There is less research evidence on the lives of individuals with Edwards' and Patau's syndromes and their families than there is for Down's syndrome. However, there is evidence that many parents whose baby survives the initial neonatal period report a positive view of family life and the quality of life of their child.¹⁶

A brief history of prenatal testing and screening

- 1.9 In 1968, Down's syndrome was detected in a fetus for the first time using amniocentesis, a procedure that involves inserting a needle through the woman's abdomen into the amniotic sac and extracting a sample of amniotic fluid.¹⁷ Amniocentesis, which can be carried out accurately from approximately 15 weeks' gestation, carries a risk of miscarriage due to infection, bleeding or damage to the amniotic sac that surrounds the fetus. Amniocentesis was increasingly used throughout the 1970s for the prenatal diagnosis of various conditions.¹⁸ In the mid-1980s, chorionic villus sampling (CVS) began to be offered as part of standard antenatal care. This test, which also carries a risk of miscarriage, sampled placental material rather than fetal material within the amniotic fluid and could be carried out from approximately eleven weeks' gestation.
- 1.10 The exact level of risk of miscarriage posed by amniocentesis and CVS is contentious, and is thought to vary depending on the experience of the clinician carrying out the procedure.¹⁹ The Royal College of Obstetricians and Gynaecologists suggest that

¹² Morris JK and Springett A (2014) *The National Down Syndrome Cytogenetic Register for England and Wales: 2013 annual report* available at: http://www.binocar.org/content/annrep2013_FINAL_nologo.pdf.

¹³ NHS Scotland (2010) *Scottish perinatal and infant mortality and morbidity report*, available at: <http://www.isdscotland.org/Health-Topics/Maternity-and-Births/Publications/2012-01-31/2012-01-31-spimmr2010-report.pdf>.

¹⁴ SOFT UK (2016) *Help for families*, available at: <http://www.soft.org.uk/Help-for-Families>.

¹⁵ Carey JC (2012) Perspectives on the care and management of infants with trisomy 18 and trisomy 13: striving for balance *Current Opinion in Pediatrics* **24**: 672-8; Andrews SE, Downey AG, Showalter DS *et al.* (2016) Shared decision making and the pathways approach in the prenatal and postnatal management of the trisomy 13 and trisomy 18 syndromes *American Journal of Medical Genetics Part C, Seminars in Medical Genetics* **172**: 257-63.

¹⁶ Janvier A, Farlow B and Wilfond BS (2012) The experience of families with children with trisomy 13 and 18 in social networks *Pediatrics* **130**: 293-8.

¹⁷ Nadler H (1968) Antenatal detection of hereditary disorders *Pediatrics* **42**: 912-8.

¹⁸ Nadler HL and Gerbie AB (1970) Role of amniocentesis in the intrauterine detection of genetic disorders *New England Journal of Medicine* **282**: 596-9.

¹⁹ Royal College of Obstetricians and Gynaecologists (2010) *Green-top guideline no. 8. amniocentesis and chorionic villus sampling*, available at: https://www.rcog.org.uk/globalassets/documents/guidelines/gtg_8.pdf.

women should be informed that the additional risk of miscarriage following amniocentesis is around one per cent, and that the additional risk of miscarriage following CVS may be slightly higher than that of amniocentesis when carried out after 15 weeks' gestation.²⁰ However, other studies suggest higher and lower figures for the additional risk, which range from 0.1 to 1.4 per cent for amniocentesis and 0.2 to 1.9 per cent for CVS.²¹

- 1.11 In the 1980s, it was discovered that levels of certain proteins and hormones in the pregnant woman's blood were associated with the fetus having Down's syndrome and other congenital conditions.²² These indicators could be measured without putting the pregnancy at risk of miscarriage, using a technique referred to as 'serum screening'. By 1998, many health authorities in the UK offered serum screening for Down's syndrome in the second trimester (usually regarded as extending from the 13/14th to the 27/28th weeks of pregnancy). Some authorities offered screening to all pregnant women regardless of age; some offered it only to women over a certain age. Various iterations of serum screening were developed, most recently the 'quadruple screen', which measures levels of four biochemical markers in maternal blood serum. In 2004, it became national NHS policy in England to offer all pregnant women serum screening regardless of age (see Box 1.1 for an explanation of screening).²³

Box 1.1: What is screening?

Screening is the process of identifying people who may have an increased chance of having a condition. Having a positive screening test result does not mean the person definitely has the condition screened for; it means that their chance of having the condition is greater than the background chance. A diagnostic test will confirm whether they have the condition or not and allow for care planning to take place. For example, in England, the NHS fetal anomaly screening programme currently offers blood tests and an ultrasound scan (called the 'combined test') to all pregnant women as a screening test for Down's, Edwards' and Patau's syndrome. If a woman is given a 1 in 150 (0.67 per cent) chance result, looking at the population as a whole this means that 1 out of every 150 women who receive that result will go on to have a baby with the condition; 149 will not. Those identified as having a high chance of one of the conditions are offered CVS or amniocentesis to reach a confirmed diagnosis. NIPT is a screening test, not a diagnostic test, for Down's, Edwards' and Patau's syndromes.

- 1.12 In the mid-2000s, a 'combined' screening test for Down's syndrome in fetuses was developed that could be carried out in the first trimester. This test combines information from a serum screen with a measurement from an ultrasound scan of the nuchal fold on the back of the neck of the fetus. The current NHS fetal anomaly screening programme offers the combined screening test to all pregnant women in England, Wales and Scotland between 10 and 14 weeks, or the quadruple screen to women who require

²⁰ *ibid.*

²¹ O'Leary P, Maxwell S, Murch A and Hendrie D (2013) Prenatal screening for Down syndrome in Australia: costs and benefits of current and novel screening strategies *Australian and New Zealand Journal of Obstetrics and Gynaecology* **53**: 425-33; Tabor A, Vestergaard CH and Lidegaard O (2009) Ultrasound in Obstetrics and Gynecology *Ultrasound in Obstetrics and Gynecology* **34**: 19-24; Akolekar R, Beta J, Picciarelli G, Ogilvie C and D'Antonio F (2015) Procedure-related risk of miscarriage following amniocentesis and chorionic villus sampling: a systematic review and meta-analysis *Ultrasound in Obstetrics and Gynecology* **45**: 16-26

²² Wald NJ, Cuckle HS, Densem JW *et al.* (1988) Maternal serum screening for Down's syndrome in early pregnancy *British Medical Journal* **297**: 883-7.

²³ Harcombe J and Armstrong V (2008) Antenatal screening. The UK NHS antenatal screening programmes: policy and practice *InnovAiT* **1**: 579-88.

screening in the second trimester.²⁴ In Northern Ireland, there is little information available on the provision of screening for Down's syndrome, and a 2010 survey of maternity units found that the combined test was not offered consistently to all pregnant women across the region.²⁵ All 'screen positive' results need to be confirmed by an invasive diagnostic test. Women who are found to have between a 1 in 2 (50 per cent) and a 1 in 150 (0.67 per cent) chance of having a fetus with Down's syndrome through screening are offered CVS or amniocentesis to reach a confirmed diagnosis. Box 1.2 sets out some approximate performance statistics for the combined test, which suggests approximately 9 out of 10 women receiving a high chance result will not have a fetus with Down's syndrome.

Box 1.2: Performance of the combined test

There is no definitive research or national data on the performance of the combined test for Down's, Edwards' and Patau's syndromes. Drawing on data generated by two studies and assuming that there will be 286 fetuses with Down's syndrome among 100,000 pregnant women, we suggest the following approximate estimations of how well the combined test performs for Down's syndrome and for Down's, Edwards' and Patau's syndromes together. It should be noted that the threshold for positive results for the combined test is designed to be women with a $\geq 1/150$ or $\geq 1/270$ chance of having a fetus with one of the conditions, so the chosen threshold will, by its nature, include a large number of false positives.²⁶

	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %
Combined test for Down's syndrome	84	98	10.7	99.95
Combined test for Down's, Edwards' and Patau's syndromes	84	98	13	>99.9

Notes

- **Sensitivity** is what proportion of affected cases will be identified as screen-positive by the test.
- **Specificity** is what proportion of unaffected cases will be identified as screen-negative by the test.
- **Positive predictive value** is what proportion of the screen-positive cases are in fact affected.
- **Negative predictive value** is what proportion of the screen-negative cases are in fact unaffected.

When referring to the **accuracy** of NIPT in this report, we are referring generally to the specificity, sensitivity, positive predictive value and negative predictive value of the test. It should be noted that the term accuracy is sometimes used in other literature to refer to a specific calculation i.e. (the number of true positives + the number of true negatives) / the total number of results. In this context, that definition may be unhelpful if it distracts attention from poor test performance indicated by the positive predictive value.

²⁴ NHS England (April 2015) *Fetal anomaly screening programme handbook for ultrasound practitioners*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/443865/FASP_ultrasound_handbook_July_2015_090715.pdf; NHS Scotland (2015) *National protocols: fetal anomaly and Down's syndrome screening* available at: <http://www.nsd.scot.nhs.uk/Documents/2015%20-%20Fetal%20Anomaly%20and%20Down's%20Syndrome%20Screening%20Protocols%20-%20v%201.pdf>.

²⁵ Lynn F, McNeill J and Alderdice F (2010) Current trends in antenatal screening services: results from a regional survey *The Ulster Medical Journal* **79**: 12-5.

²⁶ Wald NJ and Bestwick JP (2015) Performance of antenatal reflex DNA screening for Down's syndrome *Journal of Medical Screening* **22**: 168-74; Taylor-Phillips S, Freeman K, Geppert J et al. (2015) *Systematic review and cost-consequence assessment of cell-free DNA testing for T21, T18 and T13 in the UK – final report*, available at: https://legacyscreening.phe.org.uk/policydb_download.php?doc=552.

- 1.13 In 2011, 74 per cent of pregnant women accessing NHS services in England and Wales opted for Down's syndrome screening, although uptake varied widely across hospital trusts and in different parts of the country.²⁷ Improvements in screening methods have led to an increase in the number of prenatal diagnoses of Down's syndrome in fetuses over the past 25 years (during which time the total number of live births in England and Wales has fluctuated between approximately 570,000 and 720,000 per year).²⁸ For example, in 1989, 318 fetuses were diagnosed with Down's syndrome, and in 2012, there were 1257 such diagnoses.²⁹ The proportion of women having a termination after a diagnosis has remained steady, ranging from 89 to 95 per cent between 1989 and 2012,³⁰ meaning that the actual number of terminations has increased. However, the number of live births of babies with Down's syndrome has remained fairly constant. This is likely to be due to an increased incidence of Down's syndrome in fetuses caused by an increase in the average age of women at delivery.³¹
- 1.14 The ultrasound scan that is offered to pregnant women at 18-20 weeks of pregnancy looks for a range of physical anomalies in the fetus and eleven specific conditions, including Edwards' and Patau's syndromes. From 2015, screening for Edwards' and Patau's syndromes was offered to all pregnant women as part of the 10-14-week combined screening test.³² Women can choose to screen for Down's syndrome only, for Edwards' and Patau's only, or for all three syndromes. The number of prenatal diagnoses per year of Edwards' syndrome ranged from around 320 to 487 in England and Wales between 2004 and 2012. For Patau's syndrome, prenatal diagnoses ranged from around 133 to 215. In 2013, the proportions of women who had terminations after a prenatal diagnosis of Edwards' and Patau's syndromes were 76 and 72 per cent, respectively.³³
- 1.15 Research has identified factors that contribute to a pregnant woman's decision to have Down's syndrome screening or testing. These include a desire for reassurance that their fetus does not have Down's syndrome; wanting to be able to prepare for a baby with Down's syndrome; enabling them to prepare for a possible diagnosis and to subsequently terminate early in a pregnancy; perceiving themselves to have an increased chance of having a baby with the condition; trust in the medical profession so perceiving the offer of a test as advised by doctors; personal experience of Down's syndrome; a negative attitude towards or fear of Down's syndrome or disability; curiosity; pressure from a partner; and feeling a responsibility to produce a 'normal' baby.³⁴ Some

²⁷ NHS Fetal Anomaly Screening Programme (2012) *Annual report 2011–2012*, available at: <http://anr-dpn.vjf.cnrs.fr/sites/default/files/FASPAAnnualReport2012-13-ok.pdf>. Down's syndrome screening uptake statistics in Scotland or Northern Ireland could not be identified. However, the National Services Division claims that 34,768 expectant mothers in Scotland were screened for Down's syndrome in 2010-2011. It is worth noting, however, that such statistics do not represent all procedures in Scotland, since they are limited to those collected by nationally designated laboratories. See: NHS Scotland (2011) *National Services Division annual report 2010/11* available at: <http://www.nsd.scot.nhs.uk/Documents/2010-11NSDAnnRep.pdf>.

²⁸ Office for National Statistics (2016) *Births in England and Wales: 2015*, available at: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthsummarytablesenglandandwales/2015>.

²⁹ Morris JK and Springett A (2014) *The National Down Syndrome Cytogenetic Register for England and Wales: 2013 annual report* available at: http://www.binocar.org/content/annrep2013_FINAL_nologo.pdf.

³⁰ *ibid.*

³¹ Loane M, Morris JK, Addor MC *et al.* (2013) Twenty-year trends in the prevalence of Down syndrome and other trisomies in Europe: impact of maternal age and prenatal screening *European Journal of Human Genetics* **21**: 27-33.

³² Public Health England (2015) *NHS screening programmes in England*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/574716/Screening_in_England_2014_to_2015.pdf.

³³ Morris JK and Springett A (2014) *The National Down Syndrome Cytogenetic Register for England and Wales: 2013 annual report* available at: http://www.binocar.org/content/annrep2013_FINAL_nologo.pdf.

³⁴ Bryant LD, Green JM and Hewison J (2010) The role of attitudes towards the targets of behaviour in predicting and informing prenatal testing choices *Psychology and Health* **25**: 1175-94; Etchegary H, Potter B, Howley H *et al.* (2008) The influence of

women accept screening because it is perceived to be a routine part of prenatal care, and in these cases it might be better described as an instance of conformity rather than active choice.³⁵ Factors affecting a woman's decision not to have screening or testing include the risk of miscarriage associated with invasive testing; the inaccuracy of the screening test; perceiving themselves to have a low chance of having a baby with Down's syndrome; lack of trust in the medical profession; the potential emotional impact of medical intervention; negative views of screening in significant others; personal experience of people with Down's syndrome; personal and religious views on the value of children with Down's syndrome; no intention to have a termination; and objection to termination on any grounds.³⁶ The individual decision-making processes in the context of screening and testing for Down's syndrome involve any number of these factors,³⁷ and these can vary depending on the cultural context.³⁸ In terms of the psychological effects of undergoing screening for Down's syndrome, several studies report that this can prompt feelings of anxiety among expectant parents before, during, and after screening. This anxiety is generally considered acute following a higher-chance result and while awaiting the results of a diagnostic test.³⁹

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- experiential knowledge on prenatal screening and testing decisions *Genetic Testing* **12**: 115-24; Garcia E, Timmermans DR and van Leeuwen E (2008) The impact of ethical beliefs on decisions about prenatal screening tests: searching for justification *Social Science and Medicine* **66**: 753-64; van den Berg M, Timmermans DR, Kleinveld JH *et al.* (2005) Accepting or declining the offer of prenatal screening for congenital defects: test uptake and women's reasons *Prenatal diagnosis* **25**: 84-90; Helm DT, Miranda S and Chedd NA (1998) Prenatal diagnosis of Down syndrome: mothers' reflections on supports needed from diagnosis to birth *Mental Retardation* **36**: 55-61; Jaques AM, Bell RJ, Watson L and Halliday JL (2004) People who influence women's decisions and preferred sources of information about prenatal testing for birth defects *Australian and New Zealand Journal Obstetrics and Gynaecology* **44**: 233-8; Gottfredsdottir H, Sandall J and Bjornsdottir K (2009) 'This is just what you do when you are pregnant': a qualitative study of prospective parents in Iceland who accept nuchal translucency screening *Midwifery* **25**: 711-20; Williams C, Sandall J, Lewando-Hundt G *et al.* (2005) Women as moral pioneers? Experiences of first trimester antenatal screening *Social Science and Medicine* **61**: 1983-92; Chiang HH, Chao YM and Yuh YS (2006) Informed choice of pregnant women in prenatal screening tests for Down's syndrome *Journal of Medical Ethics* **32**: 273-7; Garcia E, Timmermans DR and van Leeuwen E (2012) Parental duties and prenatal screening: does an offer of prenatal screening lead women to believe that they are morally compelled to test? *Midwifery* **28**: e837-43; Williams C, Sandall J, Lewando-Hundt G *et al.* (2005) Women as moral pioneers? Experiences of first trimester antenatal screening *Social Science and Medicine* **61**: 1983-92; Remennick L (2006) The quest for the perfect baby: why do Israeli women seek prenatal genetic testing? *Sociology of Health and Illness* **28**: 21-53; Kaiser AS, Ferris LE, Katz R *et al.* (2004) Psychological responses to prenatal NTS counseling and the uptake of invasive testing in women of advanced maternal age *Patient Education and Counseling* **54**: 45-53; Barr O and Skirton J (2013) Informed decision making regarding antenatal screening for fetal abnormality in the United Kingdom: a qualitative study of parents and professionals *Nursing and Health Science* **15**: 318-25; Landsman G (2009) *Reconstructing motherhood and disability in the age of 'perfect' babies: lives of mothers and infants and toddlers with disabilities* (New York: Routledge); Thomas GM (2017) *Down's syndrome screening and reproductive politics: care, choice, and disability in the prenatal clinic* (Oxford: Routledge).
- ³⁵ Pilnick A (2004) 'It's just one of the best tests that we've got at the moment': the presentation of nuchal translucency screening for fetal abnormality in pregnancy *Discourse & Society* **15**: 451-65; Santalahti P, Hemminki E, Latikka AM and Ryyanen M (1998) Women's decision-making in prenatal screening *Social Science and Medicine* **46**: 1067-76; Skirton J and Barr O (2007) Influences on uptake of antenatal screening for Down syndrome: a review of the literature *Evidence-Based Midwifery* **5**: 4-10.
- ³⁶ Bryant LD, Green JM and Hewison J (2010) The role of attitudes towards the targets of behaviour in predicting and informing prenatal testing choices *Psychology and Health* **25**: 1175-94; McNeill J, Alderdice F, Rowe R, Martin D and Dornan JC (2009) Down's syndrome screening in Northern Ireland: women's reasons for accepting or declining serum testing *Evidence Based Midwifery* **7**: 76-83; van den Berg M, Timmermans DR, Kleinveld JH *et al.* (2005) Accepting or declining the offer of prenatal screening for congenital defects: test uptake and women's reasons *Prenatal diagnosis* **25**: 84-90; Liampittong P, Halliday JL, Warren R, Watson F and Bell RJ (2003) Why do women decline prenatal screening and diagnosis? Australian women's perspective *Women Health* **37**: 89-108; Markens S, Browner CH and Press N (1999) 'Because of the risks': how US pregnant women account for refusing prenatal screening *Social Science and Medicine* **49**: 359-69; Pilnick AM, Fraser DM and James DK (2004) Presenting and discussing nuchal translucency screening for fetal abnormality in the UK *Midwifery* **20**: 82-93; Gottfredsdottir H, Bjornsdottir K and Sandall J (2009) How do prospective parents who decline prenatal screening account for their decision? A qualitative study *Social Science and Medicine* **69**: 274-7; Garcia E, Timmermans DR and van Leeuwen E (2008) The impact of ethical beliefs on decisions about prenatal screening tests: searching for justification *Social Science and Medicine* **66**: 753-64; Etchegary H, Potter B, Howley H *et al.* (2008) The influence of experiential knowledge on prenatal screening and testing decisions *Genetic Testing* **12**: 115-24.
- ³⁷ Reid B, Sinclair M, Barr O, Dobbs F and Crealey G (2009) A meta-synthesis of pregnant women's decision-making processes with regard to antenatal screening for Down syndrome *Social Science and Medicine* **69**: 1561-73.
- ³⁸ Li G, Chandrasekharan S and Allyse M (2017) "The top priority is a healthy baby": narratives of health, disability, and abortion in online pregnancy forum discussions in the US and China *Journal of Genetic Counseling* **26**: 32-9.
- ³⁹ Green JM, Hewison J, Bekker HL, Bryant LD and Cuckle HS (2004) Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review *Health Technology Assessment* **8**: iii, ix-x, 1-109; Green J and Statham H (1996)

- 1.16 Research has explored the factors that influence women's decisions to continue or terminate a pregnancy following a diagnosis. Reasons for continuing a pregnancy after a diagnosis include religious beliefs; not wanting to experience a termination; seeing the fetus on a monitor and feeling movement or a heartbeat; previous infertility; and positive attitudes towards people with Down's syndrome.⁴⁰ A common reason for terminating a pregnancy is the perceived burden of a disabled child on the woman, her partner, existing children and other family members.⁴¹ Other reasons for terminating a pregnancy include the perception that a child will have a reduced quality of life; the prognosis for the person with Down's syndrome being too uncertain; concerns about what will happen to the child after the parents have died; and negative personal or societal attitudes towards disability.⁴² Most studies have found that support from partners, family, friends, professionals and others also influences the decision to continue or terminate a pregnancy.
- 1.17 Deciding to terminate a pregnancy following diagnosis of fetal anomaly is frequently described by pregnant women and couples as shocking, painful and distressing, with some reporting feeling unprepared for making such a decision.⁴³ Research in The Netherlands found that a significant number of women experienced post-traumatic stress symptoms and depression in the 16 months following the termination, particularly among those who felt high levels of doubt during the decision-making period, lacked partner

Psychosocial aspects of prenatal screening and diagnosis, in *The troubled helix: social and psychological implications of the new human genetics*, Marteau T, and Richards M (Editors) (New York: Cambridge University Press), pp107-120; Pilnick AM, Fraser DM and James DK (2004) Presenting and discussing nuchal translucency screening for fetal abnormality in the UK *Midwifery* **20**: 82-93.

- ⁴⁰ Ahmed S, Bryant LD, Ahmed M, Jafri H and Raashid Y (2013) Experiences of parents with a child with Down syndrome in Pakistan and their views on termination of pregnancy *Journal of Community Genetics* **4**: 107-14; Bell M and Stoneman Z (2000) Reactions to prenatal testing: reflection of religiosity and attitudes toward abortion and people with disabilities *American Journal of Mental Retardation* **105**: 1-13; Bryant L, Hewison JD and Green JM (2005) Attitudes towards prenatal diagnosis and termination in women who have a sibling with Down's syndrome *Journal of Reproductive and Infant Psychology* **23**: 181-98; Helm DT, Miranda S and Chedd NA (1998) Prenatal diagnosis of Down syndrome: mothers' reflections on supports needed from diagnosis to birth *Mental Retardation* **36**: 55-61; Lawson KL (2006) Expectations of the parenting experience and willingness to consider selective termination for Down Syndrome *Journal of Reproductive and Infant Psychology* **24**: 43-59; Lawson KL and Walls-Ingram SA (2010) Selective abortion for Down syndrome: The relation between the quality of intergroup contact, parenting expectations, and willingness to terminate *Journal of Applied Social Psychology* **40**: 554-78; Leung TN, Ching Chau MM, Chang JJ *et al.* (2004) Attitudes towards termination of pregnancy among Hong Kong Chinese women attending prenatal diagnosis counselling clinic *Prenatal diagnosis* **24**: 546-51; Tymstra T, Bosboom J and Bouman K (2004) Prenatal diagnosis of Down's Syndrome: Experiences of women who decided to continue with the pregnancy *International Journal of Risk and Safety in Medicine* **16**: 91-6; Skotko BG (2005) Prenatally diagnosed Down syndrome: mothers who continued their pregnancies evaluate their health care providers *American Journal of Obstetrics and Gynecology* **192**: 670-7.
- ⁴¹ Bryant L, Hewison JD and Green JM (2005) Attitudes towards prenatal diagnosis and termination in women who have a sibling with Down's syndrome *Journal of Reproductive and Infant Psychology* **23**: 181-98; Britt DW, Risinger ST, Miller V *et al.* (2000) Determinants of parental decisions after the prenatal diagnosis of down syndrome: bringing in context *American Journal of Medical Genetics Part A* **93**: 410-6; Korenromp MJ, Page-Christiaens GC, van den Bout J, Mulder EJ and Visser GH (2007) Maternal decision to terminate pregnancy in case of Down syndrome *American Journal of Obstetrics and Gynecology* **196**: 149.e1-11; Lawson KL (2006) Expectations of the parenting experience and willingness to consider selective termination for Down Syndrome *Journal of Reproductive and Infant Psychology* **24**: 43-59; Lawson KL and Walls-Ingram SA (2010) Selective abortion for Down syndrome: The relation between the quality of intergroup contact, parenting expectations, and willingness to terminate *Journal of Applied Social Psychology* **40**: 554-78; Roberts CD, Stough LD and Parrish LH (2002) The role of genetic counseling in the elective termination of pregnancies involving fetuses with disabilities *The Journal of Special Education* **36**: 48-55.
- ⁴² Korenromp MJ, Page-Christiaens GC, van den Bout J, Mulder EJ and Visser GH (2007) Maternal decision to terminate pregnancy in case of Down syndrome *American Journal of Obstetrics and Gynecology* **196**: 149.e1-11; Lawson KL (2006) Expectations of the parenting experience and willingness to consider selective termination for Down Syndrome *Journal of Reproductive and Infant Psychology* **24**: 43-59; Statham H, Solomou W and Chitty L (2000) Prenatal diagnosis of fetal abnormality: psychological effects on women in low-risk pregnancies *Baillieres Best Practice and Research: Clinical Obstetrics Gynaecology* **14**: 731-47.
- ⁴³ Hunt K, France E, Ziebland S, Field K and Wyke S (2009) 'My brain couldn't move from planning a birth to planning a funeral': a qualitative study of parents' experiences of decisions after ending a pregnancy for fetal abnormality *International Journal of Nursing Studies* **46**: 1111-21.

support, were religious, and were at more advanced stages of pregnancy.⁴⁴ Some research suggests termination for fetal anomaly in the second trimester is associated with higher levels of stress compared with first trimester terminations;⁴⁵ other research did not find that terminating at earlier stages of gestation improved emotional well-being for the woman.⁴⁶ Adverse psychological effects reduced over time for most women in the research and although a small number of women did report regretting their decision to have a termination, most did not.⁴⁷

NIPT for Down's, Edwards' and Patau's syndromes

- 1.18 NIPT for Down's, Edwards' and Patau's syndromes works by counting the number of cfDNA fragments from the different chromosomes present in the mother's blood during pregnancy. If the fetus has one of these syndromes, there will be slightly more sequences that map to chromosome 21, 18 or 13 than expected. Different test manufacturers use slightly different testing methods,⁴⁸ but all give a very accurate prediction of whether the fetus has one of these conditions compared to existing screening tests. False positive and false negative results can occur, however, although in much smaller numbers than for the combined screening test. Some false positive results are thought to be caused by confined placental mosaicism, in which some placental cells – which are where the non-maternal fraction of the cfDNA analysed in NIPT originates – are anomalous, even though the fetus is unaffected. CfDNA from a 'vanishing twin' and genetic anomalies in the mother not previously identified may also cause false positive results. False negative results, though rare, can also occur. In some cases, this may be due to there being insufficient cfDNA from placental material present in the mother's bloodstream. Therefore, NIPT for Down's, Edwards' and Patau's syndromes is not diagnostic, and a positive result requires an invasive test to confirm whether the fetus has the condition or not.⁴⁹
- 1.19 The background chance of the conditions occurring affects how well NIPT predicts whether or not a fetus has Down's, Edwards' or Patau's syndromes in a particular situation. For example, in women who have at least a 1 in 150 (0.67 per cent) chance of having a fetus with Down's syndrome determined from combined screening, and then a high chance NIPT result, approximately 91 per cent will go on to receive a confirmed diagnosis. In a population of women who have a positive NIPT result without prior screening, this proportion is lower, at approximately 82 per cent. This means that among 500 such women who have a high chance NIPT result, 90 will not have a fetus with Down's syndrome. NIPT has been found to be less accurate in twin pregnancies: the sensitivity of NIPT in twin pregnancies is suggested to be 8.3 per cent (8 in 100 cases)

⁴⁴ Korenromp MJ, Page-Christiaens GC, van den Bout J *et al.* (2007) A prospective study on parental coping 4 months after termination of pregnancy for fetal anomalies *Prenatal diagnosis* **27**: 709-16; Korenromp MJ, Page-Christiaens GC, van den Bout J, Mulder EJ and Visser GH (2009) Adjustment to termination of pregnancy for fetal anomaly: a longitudinal study in women at 4, 8, and 16 months *American Journal of Obstetrics and Gynecology* **201**: 160.e1-7.

⁴⁵ Daugirdaite V, van den Akker O and Purewal S (2015) Posttraumatic stress and posttraumatic stress disorder after termination of pregnancy and reproductive loss: a systematic review *Journal of Pregnancy* **2015**: 646345.

⁴⁶ Statham H, Solomou W and Chitty L (2000) Prenatal diagnosis of fetal abnormality: psychological effects on women in low-risk pregnancies *Baillieres Best Practice and Research: Clinical Obstetrics Gynaecology* **14**: 731-47.

⁴⁷ Korenromp MJ, Page-Christiaens GC, van den Bout J *et al.* (2007) A prospective study on parental coping 4 months after termination of pregnancy for fetal anomalies *Prenatal diagnosis* **27**: 709-16; Korenromp MJ, Page-Christiaens GC, van den Bout J, Mulder EJ and Visser GH (2009) Adjustment to termination of pregnancy for fetal anomaly: a longitudinal study in women at 4, 8, and 16 months *American Journal of Obstetrics and Gynecology* **201**: 160.e1-7.

⁴⁸ Royal College of Obstetricians and Gynaecologists (2014) *Non-invasive prenatal testing for chromosomal abnormality using maternal plasma DNA. Scientific impact paper No. 15*, available at: https://www.rcog.org.uk/globalassets/documents/guidelines/sip_15_04032014.pdf.

⁴⁹ Taylor-Phillips S, Freeman K, Geppert J *et al.* (2015) *Systematic review and cost-consequence assessment of cell-free DNA testing for T21, T18 and T13 in the UK – final report*, available at: https://legacyscreening.phe.org.uk/policydb_download.php?doc=552.

lower than in singleton pregnancies.⁵⁰ Box 1.3 provides the latest performance data for NIPT for Down's, Edwards' and Patau's syndromes in different populations.

Box 1.3: Warwick Evidence systematic review of performance of NIPT

A systematic review of clinical studies on the performance of NIPT for Down's, Edwards' and Patau's syndromes was published in 2016 by Warwick Evidence. The 41 studies included in the review were mainly carried out by commercial companies and some involved more than 100,000 pregnant women. The review looked at the performance of NIPT both in women with an increased prior chance of carrying a fetus with one of the conditions (which was defined in different ways in the studies included in the review) and in the general population of pregnant women.⁵¹

	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %
NIPT for Down's syndrome in high chance population	97.3	99.7	91.3	99.91
NIPT for Down's syndrome in general population	95.9	99.9	81.6	99.98
NIPT for Edwards' syndrome in high chance population	93	99.7	84	99.89
NIPT for Edwards' syndrome in general population	86.5	99.8	37	99.99
NIPT for Patau's syndrome in high chance population	95	99.9	87	99.97
NIPT for Patau's syndrome in general population	77.5	>99.9	49	99.99

See Box 1.2, p8, for definitions of sensitivity, specificity, positive predictive value and negative predictive value.

- 1.20 There is a possibility of test failure with NIPT, in which no useable results are produced. The rate of test failure of NIPT for Down's, Edwards' and Patau's syndromes has been found to range from 0 to 13 per cent depending on the study.⁵² There is some evidence that the rate of test failure is higher at earlier gestational ages and in obese women, in whom the concentration of cfDNA in the woman's blood is lower, as well as in aneuploid pregnancies. Some NIPT providers take account of the 'fetal fraction' in their analysis, which is the amount of cfDNA in the maternal blood that is of fetal origin. This can allow a fetal fraction threshold to be set, which must be reached before a result is given; if it is

⁵⁰ Taylor-Phillips S, Freeman K, Geppert J *et al.* (2016) Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis *BMJ Open* 6: e010002.

⁵¹ *ibid.*

⁵² *ibid.*

not reached, a result of 'failed' may be given.⁵³ In comparison, although more false positive results arise from the combined screening test, it very rarely fails to produce a result. Inconclusive or indeterminate results can also occur with NIPT, which happens when the result is in a middle-range which is neither positive nor negative. The rate of indeterminate results has been found to range from 0 to 11 per cent.⁵⁴

- 1.21 NIPT for Down's, Edwards' and Patau's syndromes has been available in the private sector in the UK since 2012 (see Chapter 4). The Department of Health has recently announced that pregnant women who are found to have at least a 1 in 150 (0.67 per cent) chance of having a fetus with any of these conditions following the combined screening test will be offered NIPT in the NHS from 2018 (see Chapter 2).
- 1.22 Research has explored pregnant women's attitudes towards the use of NIPT for screening fetuses for Down's, Edwards' and Patau's syndrome. Many women were found to view NIPT as a positive development in prenatal care. The advantages of NIPT were thought to be its safety and accuracy, and the ability to have NIPT at an early stage of pregnancy, which would allow pregnant women and couples to make informed choices about their pregnancy earlier. However, women also raised concerns about NIPT, including the possibility of prenatal testing becoming routine or trivial, women feeling pressure to have NIPT because there is no miscarriage risk, concerns about the effects on disabled people if the test becomes routine, and the potential expansion of NIPT to test for non-medical traits.⁵⁵
- 1.23 In the UK, media coverage of NIPT has focused on the proposal to offer NIPT for Down's syndrome to some pregnant women in the NHS. Coverage initially centred on the potential for offering NIPT to lower the number of miscarriages caused by invasive diagnostic procedures.⁵⁶ Attention moved to the potential for offering NIPT to lead to an increase in terminations of fetuses with Down's syndrome and concerns that people with Down's syndrome could be 'screened out'.⁵⁷ A BBC2 documentary entitled 'A world without Down's syndrome?', which considered some of the issues raised by the introduction of NIPT for Down's syndrome in the NHS, was aired in October 2016.⁵⁸ The documentary was presented by actor Sally Phillips who has a son with Down's

⁵³ Personal communication with Illumina.

⁵⁴ Taylor-Phillips S, Freeman K, Geppert J *et al.* (2016) Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis *BMJ Open* **6**: e010002.

⁵⁵ Lau JY, Yi H and Ahmed S (2016) Decision-making for non-invasive prenatal testing for Down syndrome: Hong Kong Chinese women's preferences for individual vs relational autonomy *Clinical Genetics* **89**: 550-6; Lewis C, Hill M, Skirton H and Chitty LS (2016) Development and validation of a measure of informed choice for women undergoing non-invasive prenatal testing for aneuploidy *European Journal of Human Genetics* **24**: 809-16; Lewis C, Hill M and Chitty LS (2016) Women's experiences and preferences for service delivery of non-invasive prenatal testing for aneuploidy in a public health setting: A mixed methods study *PloS one* **11**: e0153147; Li WH, Wang PH, Chuang CM *et al.* (2015) Noninvasive prenatal testing for fetal trisomy in a mixed risk factors pregnancy population *Taiwan Journal of Obstetrics and Gynecology* **54**: 122-5; O'Brien BM, Kloza EM, Halliday JV, Lambert-Messerlian GM and Palomaki GE (2014) Maternal plasma DNA testing: experience of women counseled at a prenatal diagnosis center *Genetic Testing and Molecular Biomarkers* **18**: 665-9; Yi H, Hallowell N, Griffiths S and Yeung Leung T (2013) Motivations for undertaking DNA sequencing-based non-invasive prenatal testing for fetal aneuploidy: a qualitative study with early adopter patients in Hong Kong *PloS one* **8**: e81794; Strange H (2015) Non-invasive prenatal diagnosis and testing: perspectives on the emergence and translation of a new prenatal testing technology. PhD Thesis, Cardiff University, available at: https://orca.cf.ac.uk/90887/2/Heather%20Strange_Thesis_Final%20Version_27_04_16%20Signed.pdf.

⁵⁶ See, for example: BBC (6 June 2015) *Down's blood test 'would cut risk of miscarriage'*, available at: <http://www.bbc.co.uk/news/health-33025227>.

⁵⁷ See, for example: The Telegraph (18 January 2016) *Down's syndrome people risk 'extinction' at the hands of science, fear and ignorance*, available at: <http://www.telegraph.co.uk/news/2016/03/22/downs-syndrome-people-risk-extinction-at-the-hands-of-science-fe/>; The Sun (11 August 2016) *Families tell of fears 99% accurate Down's syndrome test could lead to rise in abortions*, available at: <https://www.thesun.co.uk/news/1591048/families-tell-of-fears-99-accurate-downs-syndrome-test-could-lead-to-rise-in-abortions/>.

⁵⁸ See: <http://www.bbc.co.uk/programmes/b07ycbj5>.

syndrome. It generated a large amount of media debate on the topic,⁵⁹ and drew attention to screening practices in other countries, such as Iceland, where uptake of screening among pregnant women and termination rates following a diagnosis of Down's syndrome are reportedly very high.

Prenatal testing for other genetic conditions and traits

- 1.24 There are many other genetic conditions that can arise at conception, but these tend to be rarer and are not specifically screened for in pregnancy. Indicators that suggest a fetus might have a rare genetic condition might be seen on a fetal anomaly ultrasound scan, however, and the woman may be referred for further investigation and genetic testing. Pregnant women and couples with a family history of a genetic condition may also seek prenatal genetic testing services if they want to find out whether their child has inherited the condition. Previously, genetic testing often involved an invasive diagnostic procedure such as amniocentesis or CVS. More recently, NIPT techniques have been used to develop non-invasive tests for some forms of rare genetic conditions, such as cystic fibrosis, Apert syndrome and some skeletal dysplasias.⁶⁰ NIPT for these conditions can be diagnostic, especially if the condition has arisen at conception or has been inherited from the father, which then removes the need for invasive testing. NIPT for rare genetic conditions such as these is available in the NHS through specialist genetic testing services (see Chapter 3).
- 1.25 All pregnant women are given the option of NHS screening for the inherited genetic diseases thalassemia and sickle cell anaemia.⁶¹ This involves testing first pregnant women and then the partners of those women who are found to be carriers, to establish whether they are carriers of the genes that cause thalassemia and sickle cell anaemia. When both parents are carriers, invasive diagnostic testing is offered. NIPT for determining whether a fetus has one of these conditions is not currently available, although such tests may be available for clinical use in the future.⁶²
- 1.26 NIPT can accurately determine the sex of the fetus from nine or ten weeks of pregnancy. In the private sector, sex determination is widely offered as an optional extra to women seeking NIPT for Down's, Edwards' and Patau's syndromes, and it is available on a direct-to-consumer basis from some providers. Sex determination is also available in the NHS to pregnant women who have a chance of having a fetus with a sex-linked genetic condition, such as Duchenne muscular dystrophy.⁶³ Determining the sex of the fetus using NIPT can rule out the need for invasive testing in some cases. NIPT can also be used to determine whether a pregnant woman with a rhesus D negative blood type requires medication to prevent haemolytic disease in the fetus.⁶⁴

⁵⁹ See, for example: The Huffington Post UK (6 October 2016) *Sally Phillips' Down's syndrome documentary prompts fierce debate around screening and abortion*, available at: http://www.huffingtonpost.co.uk/entry/world-without-downs-syndrome-sally-phillips-documentary-sparks-debate_uk_57f62097e4b0126526822bb6; The Oxford Mail (29 October 2016) *'Don't wipe out the next generation of children with Down's syndrome'*, available at: http://www.oxfordmail.co.uk/news/14830797._Don_t_wipe_out_the_next_generation_of_children_with_Down_s_syndrome/

⁶⁰ For more information about these conditions see: <http://www.nhs.uk/Conditions/cystic-fibrosis>, www.nhs.uk/conditions/restricted-growth and www.nhs.uk/conditions/craniosynostosis.

⁶¹ For more information about these conditions see: www.nhs.uk/conditions/Thalassaemia and <http://www.nhs.uk/conditions/sickle-cell-anaemia>.

⁶² Xiong L, Barrett AN, Hua R *et al.* (2015) Non-invasive prenatal diagnostic testing for beta-thalassaemia using cell-free fetal DNA and next generation sequencing *Prenatal diagnosis* **35**: 258-65.

⁶³ For more information about this condition see: <http://www.nhs.uk/conditions/Muscular-dystrophy>.

⁶⁴ For more information about this condition see: <http://www.nhs.uk/Conditions/Rhesus-disease>.

- 1.27 Research on the views of pregnant women and families with direct experience of genetic conditions has found widespread support for the availability of NIPT to detect rare genetic conditions. The fact that NIPT is safe, accurate, and can be carried out early in pregnancy were identified as benefits. However, concerns were raised about a possible pressure to terminate following a diagnosis and how decisions about which conditions are tested for are made.⁶⁵
- 1.28 Several private providers of NIPT offer testing for additional genetic conditions, including when the woman or couple does not have an increased chance of having a baby with one of these conditions. For example, it is possible to access through private healthcare clinics NIPT for sex aneuploidy conditions, such as monosomy X, also called Turner syndrome (when a girl has only one copy of the X chromosome), and Klinefelter syndrome (when a boy has two copies of the X chromosome and one Y chromosome).⁶⁶ NIPT for these conditions does not offer a definitive diagnosis. The performance of NIPT for sex aneuploidy is not as well studied as it is for Down's, Edwards' and Patau's syndromes, but a recent review found that NIPT for sex aneuploidy has a high failure rate, a relatively low detection rate and a high false positive rate.⁶⁷ It has been suggested that several factors exist that present barriers to the development of highly effective NIPT for sex chromosomal imbalances.⁶⁸
- 1.29 Several NIPT manufacturers also offer to test for conditions caused by 'microdeletions', which is when a tiny piece of chromosome is missing, including when the woman or couple is not already known to have an increased chance of a baby with one of these conditions. The microdeletions tested for include the 22q11.2 deletion (DiGeorge syndrome) and 5p minus (cri-du-chat syndrome).⁶⁹ The performance of NIPT for microdeletions is not well documented. A recent independent study suggested that there is uncertainty about the sensitivity of NIPT for microdeletions and that it is not yet ready for routine clinical implementation due to high false positive rates.⁷⁰ Further, a study of the views of pregnant women found that participants were concerned about the utility of

⁶⁵ Boardman FK, Young PJ and Griffiths FE (2017) Population screening for spinal muscular atrophy: A mixed methods study of the views of affected families *American Journal of Medical Genetics Part A*: 421-34; Hill M, Fisher J, Chitty LS and Morris S (2012) Women's and health professionals' preferences for prenatal tests for Down syndrome: a discrete choice experiment to contrast noninvasive prenatal diagnosis with current invasive tests *Genetic Medicine* **14**: 905-13; Hill M, Twiss P, Verhoef TI *et al.* (2015) Non-invasive prenatal diagnosis for cystic fibrosis: detection of paternal mutations, exploration of patient preferences and cost analysis *Prenatal diagnosis* **35**: 950-8; Hill M, Suri R, Nash EF, Morris S and Chitty LS (2014) Preferences for prenatal tests for cystic fibrosis: A discrete choice experiment to compare the views of adult patients, carriers of cystic fibrosis and health professionals *Journal of Clinical Medicine* **3**: 176-90; Lewis C, Hill M, Skirton H and Chitty LS (2012) Fetal sex determination using cell-free fetal DNA: service users' experiences of and preferences for service delivery *Prenatal diagnosis* **32**: 735-41; Lewis C, Hill M, Skirton H and Chitty LS (2012) Non-invasive prenatal diagnosis for fetal sex determination: benefits and disadvantages from the service users' perspective *European Journal of Human Genetics* **20**: 1127-33; Lewis C, Hill M and Chitty LS (2014) Non-invasive prenatal diagnosis for single gene disorders: experience of patients *Clinical Genetics* **85**: 336-42; Skirton H, Goldsmith L and Chitty LS (2015) An easy test but a hard decision: ethical issues concerning non-invasive prenatal testing for autosomal recessive disorders *European Journal of Human Genetics* **23**: 1004-9.

⁶⁶ For more information about these conditions see: <http://www.nhs.uk/conditions/turners-syndrome> and <http://www.nhs.uk/Conditions/klinefelters-syndrome>.

⁶⁷ Gil MM, Quezada MS, Revello R, Akolekar R and Nicolaides KH (2015) Analysis of cell-free DNA in maternal blood in screening for fetal aneuploidies: updated meta-analysis *Ultrasound in Obstetrics & Gynecology* **45**: 249-66.

⁶⁸ Benn P, Cuckle H and Pergament E (2013) Non-invasive prenatal testing for aneuploidy: current status and future prospects *Ultrasound in Obstetrics & Gynecology* **42**: 15-33.

⁶⁹ Jensen TJ, Dzakula Z, Deciu C, van den Boom D and Ehrich M (2012) Detection of microdeletion 22q11.2 in a fetus by next-generation sequencing of maternal plasma *Clinical chemistry* **58**: 1148-51; Wapner RJ, Babiarez JE, Levy B *et al.* (2015) Expanding the scope of noninvasive prenatal testing: detection of fetal microdeletion syndromes *American Journal of Obstetrics & Gynecology* **212**: 332.e1-e9. For more information about these conditions see: <http://www.nhs.uk/conditions/digeorge-syndrome> and <https://ghr.nlm.nih.gov/condition/cri-du-chat-syndrome>

⁷⁰ Lo KK, Karampetsou E, Boustred C *et al.* (2016) Limited clinical utility of non-invasive prenatal testing for subchromosomal abnormalities *American Journal of Human Genetics* **98**: 34-44.

receiving information about microdeletions that have variable or unknown effects on the future child or person.⁷¹

Future developments in NIPT

- 1.30 Research in the field is largely being driven by the international commercial NIPT sector, although research is also being funded by the public sector both in the UK and abroad. NIPT for a wider range of medical conditions or impairments is likely to be available in future. Whole genome and exome sequencing using NIPT has already been carried out in a research setting, and it is likely that our ability to interpret the vast amount of detailed information that this elicits will improve in future.
- 1.31 Scientists working in the field suggest that near-future developments in using cfDNA to predict or diagnose genetic conditions are likely to be technology-driven, and these developments may lead to increasingly sensitive analyses of tiny genetic variations or single-nucleotide polymorphisms (SNPs).⁷² This may enable tests to be developed for different kinds of medical conditions or impairments, including adult onset conditions, and for existing tests to become even more accurate. It is unlikely that it will be possible to perform NIPT much earlier than nine weeks of pregnancy in future, due to the low concentration of cfDNA in the pregnant woman's blood before this period of gestation.
- 1.32 It already has been shown that it is possible to reveal the entire fetal genome – the complete set of fetal DNA – from placental cfDNA.⁷³ This is a complicated and expensive process, and one that is performed much more readily if the complete genomic sequences of both parents are available. Whole exome sequencing has also been carried out using placental cfDNA.⁷⁴ The exome is the term given to all of the genes in a genome that code for proteins. The exome makes up less than two per cent of the genome, but is thought to harbour approximately 85 per cent of the DNA mutations that cause genetic disorders. The sensitivity of these methods for detecting genetic mutations, particularly those arising at conception, is thought to be too low for it to be considered for clinical practice at the current time.⁷⁵ However, it is likely that as next generation sequencing techniques develop, the clinical utility of prenatal whole genome or exome sequencing will increase, the cost will come down and it could be available commercially.⁷⁶
- 1.33 A key challenge of whole genome or exome sequencing will be the interpretation of the vast amount of information it could elicit. However, our capacity to interpret the

⁷¹ Agatista PK, Mercer MB, Leek AC *et al.* (2015) A first look at women's perspectives on noninvasive prenatal testing to detect sex chromosome aneuploidies and microdeletion syndromes *Prenatal diagnosis* **35**: 692-8.

⁷² Hui WW, Jiang P, Tong YK *et al.* (2017) Universal haplotype-based noninvasive prenatal testing for single gene diseases *Clinical chemistry* **63**: 513-24. A single nucleotide polymorphism, often abbreviated to SNP, is a variation in a single nucleotide that occurs at a specific position in the genome, where each variation is present to some appreciable degree within a population. For example, at a specific base position in the human genome, the base C may appear in most individuals, but in a minority of individuals, the position is occupied by base A.

⁷³ Chan KC, Jiang P, Sun K *et al.* (2016) Second generation noninvasive fetal genome analysis reveals de novo mutations, single-base parental inheritance, and preferred DNA ends *Proceedings of the National Academy of Science of the United States of America* **113**: E8159-e68; Lo YM, Chan KC, Sun H *et al.* (2010) Maternal plasma DNA sequencing reveals the genome-wide genetic and mutational profile of the fetus *Science Translational Medicine* **2**: 61ra91; Fan HC, Gu W, Wang J *et al.* (2012) Non-invasive prenatal measurement of the fetal genome *Nature* **487**: 320-4; Kitzman JO, Snyder MW, Ventura M *et al.* (2012) Noninvasive whole-genome sequencing of a human fetus *Science Translational Medicine* **4**: 137ra76.

⁷⁴ Fan HC, Gu W, Wang J *et al.* (2012) Non-invasive prenatal measurement of the fetal genome *Nature* **487**: 320-4.

⁷⁵ Mackie FL, Carss KJ, Hillman SC, Hurler ME and Kilby MD (2014) Exome sequencing in fetuses with structural malformations *Journal of Clinical Medicine* **3**: 747-62.

⁷⁶ Donley G, Hull SC and Berkman BE (2012) Prenatal whole genome sequencing *Hastings Center Report* **42**: 28-40.

significance of genetic information is likely to increase in future as research in this area develops. For example, the Prenatal Assessment of Genomes and Exomes (PAGE) study, which involves a consortium of UK-based research organisations and hospitals, aims to gain a better understanding of genetic variants causing developmental problems during pregnancy by carrying out prenatal assessments of genomes and exomes.⁷⁷

- 1.34 We explored the possibility of NIPT being used to test for neurodevelopmental disorders, such as attention deficit hyperactivity disorder (ADHD), autism and schizophrenia, in the future. Most such conditions are multifactorial, are likely to be heavily influenced by environmental factors and gene-gene interactions, and would be extremely difficult to predict with any accuracy. The same is likely to be true of behavioural traits such as intelligence, susceptibility to aggression and other forms of antisocial conduct.⁷⁸ However, recent research has suggested that it is possible to account for almost ten per cent of the variance in educational achievement by examining common SNPs.⁷⁹

Other techniques for diagnosing, treating or avoiding genetic conditions

- 1.35 NIPT is a fairly new technique in the field of prenatal genetic screening and testing. Other non-invasive methods of sampling the fetal genome are being developed, including the sampling of cells from the cervical canal.⁸⁰ Still other techniques that can reliably detect genetic conditions are widely used in situations where a woman has a family history of a genetic condition or if a screening test suggests that the fetus may have a genetic condition. Karyotyping, for example, is a test that examines the number and appearance of chromosomes in the cells of the fetus. Chromosomal microarray (CMA) is a newer technique that can detect chromosome anomalies at a greater resolution. It can detect tiny changes in the chromosome, called copy number variants, such as microdeletions, as well as anomalies in the number of chromosomes. This technique can produce findings that are difficult to interpret, such as genetic mutations that have unknown or variable effects. Professional guidance on the use of CMA in prenatal testing recommends that only findings that inform the management of the pregnancy or of the family should be reported. It is recommended that findings of uncertain significance, or those that have no 'clinically actionable consequence' for the child in the future are not reported.⁸¹ These techniques generally require samples of amniotic fluid obtained through amniocentesis or placental tissue obtained through CVS, and so differ from NIPT in that they involve an invasive procedure.
- 1.36 Very few interventions currently exist for treating genetic conditions during pregnancy following prenatal diagnosis. An exception is the use of dexamethasone in pregnant women who have a chance of carrying a female fetus affected by congenital adrenal hyperplasia.⁸² The potential for *in utero* treatments for other genetic conditions is being

⁷⁷ See: <http://www.sanger.ac.uk/science/collaboration/prenatal-assessment-genomes-and-exomes-page>.

⁷⁸ For a discussion of the ethical issues raised by genetic testing for behavioural traits see: Nuffield Council on Bioethics (2002) *Genetics and human behaviour: the ethical context*, available at: <http://nuffieldbioethics.org/wp-content/uploads/2014/07/Genetics-and-human-behaviour.pdf>.

⁷⁹ Selzam S, Krapohl E, von Stumm S *et al.* (2016) Predicting educational achievement from DNA *Molecular Psychiatry* **22**: 267-72.

⁸⁰ Jain CV, Kadam L, van Dijk M *et al.* (2016) Fetal genome profiling at 5 weeks of gestation after noninvasive isolation of trophoblast cells from the endocervical canal *Science Translational Medicine* **8**: 363re4.

⁸¹ Joint Committee on Genomics in Medicine (2015) *Recommendations for the use of chromosome microarray in pregnancy* available at: http://www.bsgm.org.uk/media/956141/g144_useofcmapregnancy_jun15.pdf.

⁸² Dreger A, Feder EK and Tamar-Mattis A (2012) Prenatal dexamethasone for congenital adrenal hyperplasia: an ethics canary in the modern medical mine *Journal of Bioethical Inquiry* **9**: 277-94. For more information on this condition see: <http://www.nhs.uk/conditions/disorders-sex-development>.

explored. For example, researchers are attempting to develop prenatal therapies that focus on brain development in fetuses with Down's syndrome.⁸³ For women and couples who are aware in advance of their pregnancy that they have or are carriers of a heritable genetic condition, it may be possible in future to use advanced genome editing techniques to treat genetic disorders shortly after fertilisation, or to edit gametes prior to fertilisation. Genetic modification of human embryos in order to treat genetic disorders is currently illegal in the UK, although techniques to prevent the transmission of mitochondrial disorders from mother to child were approved by Parliament in 2015.⁸⁴ Efficient and low-cost new genome editing techniques are making the prospect of treating genetic disorders in embryos much more likely, and this is being explored by researchers. A separate Nuffield Council on Bioethics inquiry is currently exploring the issues raised by genome editing techniques and human reproduction.⁸⁵

- 1.37 Women and couples who have or are carriers of a heritable genetic condition can have pre-implantation genetic diagnosis (PGD) if they want to avoid their children inheriting the condition. PGD can be carried out on embryos created through *in vitro* fertilisation (IVF) and is regulated by the Human Fertilisation and Embryology Act 1990, as amended by the 2008 Act. The Act states that embryo testing for treatment purposes is permitted in order to establish whether an embryo has an anomaly that might affect its capacity to result in a live birth and to avoid a significant medical condition, including sex-linked conditions. Under the Act, the Human Fertilisation and Embryology Authority (HFEA) regulates fertility clinics and laboratories, and a list of conditions for which PGD has been previously approved by the HFEA is publicly available. Selecting embryos of a particular sex for social reasons is prohibited.⁸⁶

Laws, regulations and guidance relevant to NIPT

- 1.38 In 2007, the Organisation for Economic Co-operation and Development (OECD) published guidelines setting out principles for quality assurance in molecular genetic testing for clinical purposes, including prenatal testing, directed to governments and those involved in the regulation of genetic services. The principles state that: informed consent to test should be the norm; pre- and post-test counselling should be available; personal genetic information should be subject to privacy protection; promotional and technical claims for genetic tests should accurately describe their characteristics and limitations; and the interpretation of genetic test results should be appropriate to the individual patient and clinical situation and should be based on objective evidence.⁸⁷
- 1.39 The manufacture of NIPT tests in the UK is regulated by the Medical Devices Regulations, which implement the EU In-Vitro Diagnostic Medical Devices (IVD)

⁸³ Guedj F and Bianchi DW (2013) Noninvasive prenatal testing creates an opportunity for antenatal treatment of Down syndrome *Prenatal diagnosis* **33**: 614-8.

⁸⁴ The Council published a report on this topic in 2012: Nuffield Council on Bioethics (2012) *Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review*, available at: <http://nuffieldbioethics.org/project/mitochondrial-dna-disorders/>.

⁸⁵ For a discussion of the ethical issues raised by the use of genome editing techniques, see Nuffield Council on Bioethics (2016) *Genome editing: an ethical review*, available at: <http://nuffieldbioethics.org/wp-content/uploads/Genome-editing-an-ethical-review.pdf>. Further work on the ethical issues specifically raised by genome editing and human reproduction is underway, see: <http://nuffieldbioethics.org/project/genome-editing>.

⁸⁶ Human Fertilisation and Embryology Act 1990, Sch 2, paras 1ZA(1)(c) and 12B.

⁸⁷ OECD (2007) Guidelines for quality assurance in molecular genetic testing, available at: <http://www.oecd.org/sti/biotech/38839788.pdf>.

Directive.⁸⁸ This Directive is soon to be replaced by the EU IVD Regulation, which will have direct force in the UK.⁸⁹ However, many NIPT manufacturers are based outside Europe, mainly in the USA and China, where the IVD Directive/Regulation does not apply. In addition, genetic tests that are manufactured and used in-house by health institutions, such as NHS hospitals and laboratories, are exempt from many parts of the Directive/Regulation. The UK's decision to leave the EU also throws into question the future relevance of the EU Directive/Regulation to NIPT services being carried out in the UK.

1.40 There is no UK-specific professional guidance on NIPT, although the Royal College of Obstetrics and Gynaecologists published a 'scientific impact paper' on NIPT for aneuploidies in 2014.⁹⁰ The American College of Medical Genetics and Genomics (ACMG) published a position statement on NIPT for fetal aneuploidy in July 2016. The ACMG recommendations include:

- All pregnant women should be informed that NIPT is the most sensitive screening option for traditionally screened aneuploidies.
- Accurate, balanced, up-to-date information should be provided when a fetus is diagnosed with a chromosomal or genomic variation in an effort to educate prospective parents about the condition.
- Laboratories should provide the detection rate, clinical specificity, positive predictive values and negative predictive values for conditions being screened in marketing materials and when reporting laboratory results.
- Pregnant women should be informed of the availability of NIPT for sex chromosome aneuploidies, the increased possibility of false positive results and the potential for these conditions to have a variable prognosis.⁹¹

1.41 There are laws, NHS governance procedures and professional guidance that are relevant to any kind of prenatal testing or screening in the UK, including NIPT. For example, within the NHS, the UK National Screening Committee (UKNSC) advises ministers and the NHS about all aspects of screening and supports the implementation of screening programmes. The UKNSC assesses new screening programmes against specific criteria relating to the viability, effectiveness and appropriateness of the programme.⁹² A 2015 review of the UKNSC made recommendations for improving the way in which social, ethical, and legal issues associated with screening are considered.⁹³ In January 2016, the UKNSC recommended the 'evaluative implementation' of NIPT for

⁸⁸ Part IV of The Medical Devices Regulations 2002, available at: [https://ec.europa.eu/growth/single-market/european-standards/harmonised-standards/iv-diagnostic-medical-devices_en](http://www.legislation.gov.uk/ukxi/2002/618/part/IV/made; Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices, available at: <a href=).

⁸⁹ Council of the European Union (2016) Proposal for a regulation of the European Parliament and of the Council on *in vitro* diagnostic medical devices, available at: <https://www.emergogroup.com/sites/default/files/europe-ivd-regulation-consolidated-negotiated-text.pdf>.

⁹⁰ Royal College of Obstetricians and Gynaecologists (2014) *Non-invasive prenatal testing for chromosomal abnormality using maternal plasma DNA. Scientific impact paper No. 15*, available at: https://www.rcog.org.uk/globalassets/documents/guidelines/sip_15_04032014.pdf.

⁹¹ Gregg AR, Skotko BG, Benkendorf JL *et al.* (2016) Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics *Genetics in Medicine* **18**: 1056-65.

⁹² UK National Screening Committee (2015) *Criteria for appraising the viability, effectiveness and appropriateness of a screening programme*, available at: <https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes/criteria-for-appraising-the-viability-effectiveness-and-appropriateness-of-a-screening-programme>.

⁹³ UK National Screening Committee (2015) *Review of the UK National Screening Committee (UK NSC)*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/443953/20150602_-_Final_Recommendations.pdf.

Down's, Edwards' and Patau's syndrome in the NHS fetal anomaly screening programme.⁹⁴

- 1.42 NHS service specifications outline service and quality indicators for commissioners and providers of screening services. NHS Service Specification 16 covers prenatal screening for Down's, Edwards' and Patau's syndromes in England and sets out the care pathway that pregnant women should expect and how that service should be delivered.⁹⁵ Similar specifications are set for Wales and Scotland.⁹⁶ National Institute for Health and Care Excellence (NICE) Clinical Guidance on antenatal care for uncomplicated pregnancies offers information on best practice for the clinical care of all pregnancies, including the offer of screening for fetal anomalies.⁹⁷ The NHS service specification for medical genetics covers the diagnostic and genetic counselling services provided by regional genetics centres to patients affected by or with the chance of a genetic condition.⁹⁸ The UK Genetic Testing Network (UKGTN) evaluates the scientific validity and clinical utility of new genetic tests that its member laboratories would like to offer NHS patients, mainly covering diagnostic tests for rare genetic disorders that they define as those affecting fewer than 1 in 2,000 people.⁹⁹
- 1.43 All health and social care providers in England, including private hospitals and clinics, must be registered and regulated by the Care Quality Commission (CQC) if they carry out one or more 'regulated activities' as described in the Health and Social Care Act 2008 (Regulated Activities) Regulations 2014.¹⁰⁰ The CQC inspects registered providers to assess how they are performing against fundamental standards of quality and safety set by Government, which are set out in the legislation.¹⁰¹ NIPT would fall under the regulated activity of 'diagnostic and screening procedures' but only when the test is carried out as part of the planning or delivery of an individual's treatment or care, or as part of an NHS screening programme, rather than on a one-off basis.¹⁰² Among other functions, Healthcare Improvement Scotland is responsible for regulating independent hospitals and clinics in Scotland; Healthcare Inspectorate Wales is responsible for the registration and inspection of independent healthcare providers in Wales; and the Regulation and Quality Improvement Authority registers and inspects acute hospitals in Northern Ireland.

⁹⁴ UK National Screening Committee (2016) *UK NSC non-invasive prenatal testing (NIPT) recommendation*, available at: https://legacyscreening.phe.org.uk/policydb_download.php?doc=570.

⁹⁵ NHS England (2016) *Service Specification no. 16. NHS Fetal anomaly screening programme - screening for Down's, Edwards' and Patau's Syndromes (trisomy 21, 18 & 13)*, available at: <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/04/serv-spec-16-apr16.pdf>.

⁹⁶ See NHS Wales (2017) *Antenatal screening Wales – Professional*, available at: <http://www.antenatalscreening.wales.nhs.uk/professional/home> and National Services Scotland (2016) *Pregnancy screening programmes*, available at: <http://www.nsd.scot.nhs.uk/services/screening/pregscreening/index.html>. No equivalent specifications could be found for Northern Ireland.

⁹⁷ The National Institute for Health and Care Excellence (2016) *Antenatal care for uncomplicated pregnancies. Clinical guidance CG62*, available at: <https://www.nice.org.uk/guidance/cg62>.

⁹⁸ NHS England (2013) *Service Specification E01/S/a: medical genetics (all ages)*, available at: <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2014/04/e01-med-gen.pdf>.

⁹⁹ See: <http://ukgt.nhs.uk/>.

¹⁰⁰ The Health and Social Care Act 2008 (Regulated Activities) Regulations 2014, Sch 1, s.7, available at: <http://www.legislation.gov.uk/ukdsi/2014/9780111117613/contents>.

¹⁰¹ See: Care Quality Commission (2016) *The fundamental standards*, available at: <http://www.cqc.org.uk/content/fundamental-standards>.

¹⁰² Care Quality Commission (2015) *Registration under the Health and Social Care Act 2008. The scope of the registration*, available at: http://www.cqc.org.uk/sites/default/files/20151230_100001_Scope_of_registration_guidance_updated_March_2015_01.pdf.

- 1.44 All doctors, midwives and nurses working in either the NHS or the private sector must be registered with the General Medical Council (GMC) or the Nursing and Midwifery Council (NMC). These organisations maintain a register of all doctors, nurses and midwives allowed to practice in the UK and set standards of education, training, conduct and performance. For doctors, this includes treating patients as individuals, respecting their right to reach shared decisions about their treatment and care, and doing their best to make sure all patients receive good care and treatment that will support them to live as well as possible.¹⁰³ The GMC has produced specific guidance for doctors on patient consent which they are required to follow. The guidance states that doctors must share with patients the information they want or need in order to make decisions; maximise patients' opportunities, and their ability, to make decisions for themselves; and respect patients' decisions.¹⁰⁴ The NMC requires nurses and midwives to act in partnership with those receiving care, helping them to access relevant health and social care, information and support when they need it, and to respect, support and document a person's right to accept or refuse care and treatment. They should also "make sure that any information or advice given is evidence-based, including information relating to using any healthcare products or services".¹⁰⁵ Other health and social care professionals are regulated by bodies such as the Health and Care Professions Council and the Northern Ireland Social Care Council.
- 1.45 The recent *Montgomery v. Lanarkshire Health Board* ruling of the UK Supreme Court has been widely interpreted as marking out, in law, requirements for healthcare professionals to adopt an approach that is more in line with autonomy-centred models of healthcare when seeking consent from patients for treatments and tests.¹⁰⁶ The judgment constitutes a move away from the *Bolam* test, formerly used to appraise negligence claims for failure to disclose medical risks, which states that a medical practice must be in line with the "responsible body of medical opinion".¹⁰⁷ Instead, the judgment requires that doctors take "reasonable care to ensure that the patient is aware of any material risks involved in any recommended treatment, and of any reasonable alternative or variant treatments". Material risks were said to be those that either a reasonable patient in the patient's position would regard as significant or the doctor should reasonably be aware that the particular patient would regard as significant. This marks a legal shift away from a focus on what a reasonable doctor would tell the patient, to what a reasonable patient, and the particular patient, would want to know. The judgment as a whole is couched in language emphasising patient choice and autonomy. The Supreme Court stated, for example, that patients are now widely regarded as rights-holders, rather than as passive recipients of medical care.
- 1.46 In the context of prenatal screening, this recent development in medical case law means that doctors might now be legally obliged to inform women about the availability of particular tests and treatments, as well as the risks and benefits both to the woman and her fetus, where the healthcare professional ought to that realise the woman would regard these as significant. The Supreme Court did not mention NIPT or prenatal testing, but this revised legal standard for the disclosure of information by healthcare professionals to their patients also applies when returning NIPT results to women and

¹⁰³ General Medical Council (2013) *Good medical practice*, available at: http://www.gmc-uk.org/static/documents/content/GMP_.pdf.

¹⁰⁴ General Medical Council (2008) *Consent: patients and doctors making decisions together*, available at: http://www.gmc-uk.org/Consent_English_1015.pdf_48903482.pdf.

¹⁰⁵ Nursing and Midwifery Council (2015) *The code: professional standards of practice and behaviour for nurses and midwives*, available at: <https://www.nmc.org.uk/globalassets/sitedocuments/nmc-publications/nmc-code.pdf>.

¹⁰⁶ *Montgomery v. Lanarkshire Health Board* [2015] UKSC 11.

¹⁰⁷ *Bolam v Friern Hospital Management Committee* [1957] 1 WLR 583 and *Sidaway v. Board of Governors of the Bethlem Royal Hospital* [1985] AC 871.

might be relevant to, for example, the possibility of unanticipated or secondary findings about a woman's own health.

- 1.47 Many health and social care professionals working in the private sector are members of one of the Royal Colleges, such as the Royal College of Obstetricians and Gynaecologists (RCOG), the Royal College of Midwives (RCM), the Royal College of Nursing (RCN) or other professional organisations for allied health professionals. The Royal Colleges provide continuing professional development for their members and develop guidance for clinical practice. The RCOG has published explanatory guidance for its members, who include doctors working in the NHS and the private sector, on termination for fetal anomaly. The guidance includes advice on the information and support that should be provided to women and couples following a diagnosis of fetal anomaly (see Paragraph 1.51).¹⁰⁸ The RCM has not produced specific guidance on prenatal screening or the management of pregnancies after a diagnosis of fetal anomaly, but supports learning resources offered through the NHS screening programmes.
- 1.48 Several UK laws are relevant to prenatal genetic screening and testing services. The Human Tissue Act 2004 makes it unlawful in England, Wales and Northern Ireland to store and use human tissue with the intention of its DNA being analysed, without the consent of the person from whom the tissue came.¹⁰⁹ Fetal tissue is regarded as the mother's tissue. For consent to be valid, it must be given voluntarily by an appropriately informed person who has the capacity to agree to the activity in question. International data protection laws and common law relating to medical confidentiality in the UK are relevant to the collection and storage of genetic information through NIPT. For a detailed description of issues relating to the collection, use and linkage of data in healthcare see the Nuffield Council on Bioethics' 2015 report on this topic.¹¹⁰
- 1.49 The Abortion Act 1967 states that an abortion in England, Wales or Scotland is not unlawful when a pregnancy is terminated by a registered medical practitioner and if two medical practitioners hold the belief, "in good faith", that certain grounds are met. The Act was amended by the Human Fertilisation and Embryology Act 1990, which introduced a time limit of 24 weeks of gestation on the most common ground for abortion, which is that "the continuance of the pregnancy would involve risk, greater than if the pregnancy were terminated, of injury to the physical or mental health of the pregnant woman or any existing children of her family" (section 1(1)(a)).¹¹¹ This is often referred to as the 'social ground'. A further ground for abortion, which does not have a gestational time limit, is that "there is a substantial risk that if the child were born it would suffer from such physical or mental abnormalities as to be seriously handicapped" (section 1(1)(d)).¹¹² This is often referred to as the 'fetal anomaly ground'. The Abortion Act 1967 does not extend to Northern Ireland, where abortion is only legal when it is necessary to preserve the life of the woman, or if there is a risk of real and serious adverse effect on her physical or mental health, which is either long term or permanent.¹¹³ The fact that it

¹⁰⁸ Royal College of Obstetricians and Gynaecologists (2010) *Termination of pregnancy for fetal abnormality in England, Wales and Scotland*, available at: <https://www.rcog.org.uk/globalassets/documents/guidelines/terminationpregnancyreport18may2010.pdf>.

¹⁰⁹ Part 1 of the Human Tissue Act 2004, available at: <http://www.legislation.gov.uk/ukpga/2004/30/notes/division/5/1>.

¹¹⁰ Nuffield Council on Bioethics (2015) *The collection, linking and use of data in biomedical research and health care: ethical issues* (London: Nuffield Council on Bioethics), available at: <http://nuffieldbioethics.org/project/biological-health-data/>.

¹¹¹ Abortion Act 1967, s.1(1)(a), as amended, available at: <http://www.legislation.gov.uk/ukpga/1967/87>.

¹¹² Abortion Act 1967, s.1(1)(d), as amended, available at: <http://www.legislation.gov.uk/ukpga/1967/87>.

¹¹³ Health, Social Services and Public Safety (2016) *Guidance for health and social care professionals on termination of pregnancy in Northern Ireland*, available at: <https://www.health-ni.gov.uk/sites/default/files/publications/dhssps/guidance-termination-pregnancy.pdf>.

is legal to terminate a pregnancy following a prenatal diagnosis of a ‘serious handicap’ in England, Wales and Scotland is one of the key reasons why prenatal testing is controversial. **A review of the law relevant to NIPT, such as the Abortion Act 1967 and the Human Fertilisation and Embryology Act 1990 (see Paragraph 1.37), is outside the scope of this inquiry, and the Working Group therefore takes the current law as the backdrop of its discussions and conclusions.** However, we acknowledge that the position adopted by the law is compatible only with some views on the moral status of the embryo and fetus. The law adopts a proportional or ‘gradualist’ position, because it grants increasing protection to the developing human according to four thresholds: preimplantation, implantation to 24 weeks, post-24 weeks and birth. We also acknowledge that some consider the existence of the fetal anomaly ground to be discriminatory, and this is the subject of current Parliamentary debate.¹¹⁴

1.50 Official Department of Health statistics state that 184,824 abortions took place among women resident in England and Wales in 2015. Most abortions took place before 13 weeks (92 per cent). There were 3,213 abortions (2 per cent) carried out under the fetal anomaly ground, of which 1,179 (37 per cent) were for chromosomal anomalies. Down’s syndrome was the most commonly reported chromosomal anomaly (689; 21 per cent of terminations for fetal anomaly). A total of 883 residents of Northern Ireland travelled to England or Wales to have a termination, 14 (1.6 per cent) of which were on the fetal anomaly ground.¹¹⁵ The number of terminations for Down’s syndrome in England and Wales is also recorded by the National Down’s Syndrome Cytogenetic Register (NDSCR), and this was found to be approximately twice the figure reported by the Department of Health in 2011-2013. The reasons for this are thought to include forms not being submitted to the Department of Health and the selection of another reason for abortion if it took place before 24 weeks.¹¹⁶ There were 12,082 abortions in Scotland in 2015, of which 186 abortions (2 per cent) were carried out for fetal anomaly. Seventy-eight terminations were for chromosomal anomalies including Down’s, Edwards’ and Patau’s syndromes.¹¹⁷ There were 16 terminations of pregnancy in total in Northern Ireland during 2014-2015.¹¹⁸

1.51 There is no legal definition of ‘substantial risk’ or ‘serious handicap’ as set out in the Abortion Act. RCOG guidance on termination for fetal anomaly suggests that both the size of the risk and the gravity of the ‘handicap’ are important in the scaling of severity of abnormalities, and that doctors should weigh up the following factors when reaching a decision:

- the potential for effective treatment, either *in utero* or after birth;
- on the part of the child, the probable degree of self-awareness and of ability to communicate with others;
- the suffering that would be experienced;
- the probability of being able to live alone and to be self-supportive as an adult;

¹¹⁴ See Abortion (Disability Equality) Bill [HL] 2016/17, available at: <http://services.parliament.uk/bills/2016-17/abortiondisabilityequality.html>.

¹¹⁵ Department of Health (2016) *Abortion statistics, England and Wales: 2015*, available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/570040/Updated_Abortion_Statistics_2015.pdf

¹¹⁶ Department of Health (2014) *Matching Department of Health abortion notifications and data from the National Down’s Syndrome Cytogenetic Register and recommendations for improving notification compliance*, available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/314006/data_matching_and_under_reporting_HSA4s_final_230514.pdf.

¹¹⁷ National Services Scotland (2016) *Termination of pregnancy statistics 2015*, available at: <http://www.isdscotland.org/Health-Topics/Sexual-Health/Publications/2016-05-31/2016-05-31-Terminations-Report.pdf>.

¹¹⁸ NI Department of Health, Social Services and Public Safety (2016) *Northern Ireland termination of pregnancy statistics 2014/15*, available at: <https://www.health-ni.gov.uk/sites/default/files/publications/dhssps/hs-termination-of-pregnancy-stats-14-15.pdf>.

- on the part of society, the extent to which actions performed by individuals without disability that are essential for health would have to be provided by others.

The guidance states that doctors will be better able to demonstrate that their opinions were formed in good faith if they have sought advice from appropriate specialists, such as those with knowledge of the management of the particular condition.¹¹⁹

- 1.52 RCOG concludes that it would be unrealistic to produce a definitive list of conditions that constitute ‘serious handicap’. The reasons given for this are that “the consequences of an abnormality are difficult to predict, not only for the fetus in terms of viability or residual disability but also in relation to the impact in childhood as well as on the family into which the child would be born” and that “sufficiently advanced diagnostic techniques capable of accurately defining abnormalities or of predicting the seriousness of outcomes are not currently available”. It concludes that an assessment of the seriousness of a fetal anomaly should be considered on a case-by-case appraisal, taking into account all available clinical information.¹²⁰ Further reasons for not producing a list of conditions relates to concerns that this may lead women to believe that having a termination for these conditions is normal or expected in some way, and because what might be considered a serious condition may change over time if new treatments or care options become available.
- 1.53 ‘Handicap’ is now an outdated term that is no longer in general use, but it remains enshrined in the wording of the law. **We have elected to use the term ‘significant medical condition or impairment’ in this report to describe what would be grounds for termination under Section 1(1)(d) of the Abortion Act 1967. We recognise that what constitutes a significant medical condition or impairment is a judgment that depends on several factors, including the likely level of impairment, the available treatment options, and the views of and potential impact on the family and the individual themselves. In this report, we refer to ‘less significant medical conditions or impairments’ as those that would not have a significant impact on the life of the child or family, or where remedial treatment is available, and would not usually be considered grounds for termination under Section 1(1)(d) of the Abortion Act 1967. However, it cannot always be known in advance whether a condition or impairment will have a significant impact or not, and this can only be established on a case-by-case basis taking into account those factors already described.**
- 1.54 Also relevant to prenatal screening are laws that protect human rights and promote equality for disabled people. For example, the UN Convention on the Rights of Persons with Disabilities (CRPD) sets out the equal human rights and place in society of disabled people. By ratifying the CRPD in 2009, the UK is committed to promoting and protecting the full enjoyment of human rights by disabled people and ensuring that they have full equality under the law. The Equality Act 2010, which brought together a number of pieces of legislation relating to discrimination, protects disabled people against discrimination and created the Public Sector Equality Duty in England, Scotland and Wales.¹²¹ This duty harmonises existing equality duties relating to race, gender and disability, and aims

¹¹⁹ Royal College of Obstetricians and Gynaecologists (2010) *Termination of pregnancy for fetal abnormality in England, Scotland and Wales*, available at: <https://www.rcog.org.uk/globalassets/documents/guidelines/terminationpregnancyreport18may2010.pdf>.

¹²⁰ Ibid.

¹²¹ Equality Act 2010, available at <http://www.legislation.gov.uk/ukpga/2010/15/notes/division/2>.

to integrate consideration of equality and good relations into the day-to-day business of public authorities. This includes the duty to make reasonable adjustments in order to ensure that, as far as is reasonable, a disabled worker has the same access to everything that is involved in doing and keeping a job as a non-disabled person. In Northern Ireland, the Disability Discrimination Act 1995 makes it unlawful to discriminate against disabled persons.¹²²

Ethical starting points

- 1.55 NIPT raises a broad range of ethical issues that overlap with those connected to prenatal screening and genetic testing more broadly. The development of and widening access to NIPT in the UK gives rise to some particular and distinctive ethical concerns, and many of these were raised during our survey, consultation and other evidence-gathering activities (see the Appendix for a description of the project evidence gathering activities). This section provides an introduction to the ethical rights and wrongs, and harms and benefits that are relevant to NIPT as understood in terms of the values of choice, autonomy and consent; avoidance of harm; and equality, inclusion and fairness. A fuller account of the ethical issues raised by the increasing availability and use of NIPT, and a suggested approach for considering these issues in policy making contexts can be found in Chapter 5.

Choice, autonomy and consent

- 1.56 The ethical issues raised by NIPT relate in part to choice. In healthcare, choice and the power that individuals have to make free, informed decisions about the examinations, treatments and care they receive are widely considered to be important goods. This power is often referred to as patient autonomy, or reproductive autonomy in the context of prenatal testing.
- 1.57 Autonomy itself is recognised as a basic moral or political concept of which there are a number of understandings – all of which attempt to capture what is valuable about the ability people have to direct their own lives.¹²³ Autonomy can be viewed as self-government, self-determination or as a person's capability to exercise control over, and make choices about, the course of their life.¹²⁴ Alternative views construe autonomous action as action in accordance with principle, and autonomy as closely connected to moral agency.¹²⁵ Under most understandings of autonomy, state or individual interventions that unduly restrict individual autonomy are seen as wrong.
- 1.58 Patient autonomy and informed consent are important concepts in the context of healthcare ethics, though there is disagreement as to how patient autonomy is exercised and what is involved in gaining informed consent. One prominent model of patient autonomy in bioethics construes patient choices as autonomous broadly when patients have sufficient relevant information, and their decisions are free from external

¹²² Disability Discrimination Act 1995, available at <http://www.legislation.gov.uk/ukpga/1995/50/introduction>.

¹²³ For discussions see: Christman J (2015) Autonomy in moral and political philosophy, in *The Stanford Encyclopedia of Philosophy*, Zalta, E (Editor) available at: <https://plato.stanford.edu/archives/spr2015/entries/autonomy-moral/>; Christman J (Editor) (1989) *The inner citadel: essays on individual autonomy* (New York: Oxford University Press).

¹²⁴ See, for example: Raz J (1986) *The morality of freedom* (Oxford: Clarendon); Feinberg J (1986) *Harm to self: the moral limits of the criminal law, Volume III* (New York: Oxford University Press). This ideal can be traced back to the work of John Stuart Mill, although Mill himself does not use the word 'autonomy'. (Mill JS (1869) *On liberty* (UK: Longmans, Green, Reader, and Dyer)).

¹²⁵ Gregor M (Editor) (2006) Immanuel Kant: groundwork of the metaphysics of morals, 1st Edition (Cambridge: Cambridge University Press).

influences.¹²⁶ Alternative models of 'principled autonomy' have been defended by Onora O'Neill from a broadly Kantian perspective and invoke other concepts such as mutual trust.¹²⁷

- 1.59 However, in general there is broad agreement that in order for patients to be able to give informed consent they must have access to accurate, balanced and non-directive information about the examination, test or treatment, and be able to understand and weigh up the risks and benefits of different testing and treatment options, and of no testing or treatment. The expression 'informed consent' was first used in the 1950s¹²⁸ and it is currently reflected in good practice guidance for healthcare professionals in the UK.¹²⁹ Healthcare professionals are expected to seek informed consent from patients for the examinations, treatments and tests they provide. This requires that patients have mental capacity and that they are able to understand, retain and weigh up information about healthcare options before choosing to undergo them.¹³⁰
- 1.60 In many parts of the Western world, health and social care models based on respect for patient autonomy have come to replace doctor-led or purely beneficence models, in which decision making was seen as principally the role of the doctor.¹³¹ Over time the standard of good health and social care has moved away from one in which people were seen as passive recipients of treatments and tests arranged by health and social care experts, towards a model in which people, together with healthcare professionals, make their own choices and decisions about their care. This notion is now widely seen as a basic tenet of healthcare ethics, and respect for patient autonomy is critical to the provision of quality healthcare.¹³² The recent *Montgomery v. Lanarkshire Health Board* ruling has been widely interpreted as marking out, in law, requirements for healthcare professionals to adopt an approach that is more in line with autonomy-centred models of healthcare when seeking consent from patients for treatments and tests (see Paragraph 1.45).
- 1.61 Reproductive autonomy is a more narrow notion than patient autonomy and refers to the capability men and women have to make reproductive choices about, for example, whether and when they become parents, how many children they have, and whether or not to make use of different reproductive technologies or interventions, such as assisted conception techniques and prenatal testing to access information about a fetus.¹³³

¹²⁶ Beauchamp TL and Childress JF (2001) *Principles of biomedical ethics* (Oxford: Oxford University Press).

¹²⁷ O'Neill O (2002) *Autonomy and trust in bioethics*. (Cambridge: Cambridge University Press); Stirrat GM and Gill R (2004) Autonomy in medical ethics after O'Neill *Journal of Medical Ethics* **31**: 127-30. Neil Manson and Onora O'Neill propose a 'waiver model' of informed consent (O'Neill O and Manson N (2007) *Rethinking informed consent in bioethics* (Cambridge: Cambridge University Press)). Bullock and Widdows have argued that on this model: "[...] instead of fully informed consent being viewed as a means of respecting individual autonomy informed consent is treated as a waiver of certain rights and obligations." (Bullock E and Widdows H (2011) Reconsidering consent and biobanking, in *Biobanks and tissue research* (The Netherlands: Springer), pp111-125).

¹²⁸ Faden RR, Beauchamp TL and King NMP (1986) *A history and theory of informed consent* (New York: Oxford University Press).

¹²⁹ See, for example, British Medical Association (2017) *Consent tool kit*, available at: <https://www.bma.org.uk/advice/employment/ethics/consent/consent-tool-kit> and General Medical Council (2008) *Consent: patients and doctors making decisions together*, available at: http://www.gmc-uk.org/Consent_English_1015.pdf_48903482.pdf.

¹³⁰ Good practice guidance sets out these standards for healthcare professionals in appraising capacity and gaining informed consent from patients, though it is accepted that actual clinical practice can often fall short of these standards.

¹³¹ Will JF (2011) A brief historical and theoretical perspective on patient autonomy and medical decision making: part I: the beneficence model *CHEST Journal* **139**: 669-73.

¹³² Buchanan A, Brock D, Daniels N and Wikler D (2000) *From chance to choice: genetics and justice* (Cambridge: Cambridge University Press).

¹³³ Marteau TM, Dormandy E and Michie S (2001) A measure of informed choice *Health Expectations* **4**: 99-108.

Decisions made on the basis of information revealed through prenatal test results might concern behaviour during pregnancy, the circumstances of delivery of a baby, and whether to continue or terminate a pregnancy. For people to be able to exercise reproductive autonomy they must be in a position to make informed decisions and so must have access to accurate, balanced and non-directive information relevant to choices they make during their pregnancy about the prenatal options they are given.¹³⁴

- 1.62 A broader condition on reproductive autonomy and choice is that people's decisions should not be subject to certain kinds of pressure and should be free from duress.¹³⁵ Aside from inaccurate or absent information, risks to reproductive autonomy are posed when influence is exerted on women to undergo screening or terminate pregnancies through personal, institutional or societal expectations, biases or pressures that may come from those close to the woman, health and social care professionals, or broader society. Women must be in a position to make decisions voluntarily about undergoing examinations, tests and treatments. Such considerations may be especially important if prenatal testing comes to be seen as a standard or routine part of prenatal care and declining prenatal testing proves to be more difficult where there are no 'reasons' to do so other than not wanting to undergo testing.
- 1.63 Consumer choice is also part of the wider context of NIPT, given that it is widely available through private hospitals and clinics. In the UK, outside of the NHS, many healthcare products and services are available to those with the desire and means to buy them. Genetic testing services can be purchased from private companies by those who wish to access information about their family's ancestry or genetic risk factors for certain conditions. Individuals have the freedom to make choices about how best to make use of their own resources to access goods and services available in the private sector, for health or other reasons.
- 1.64 The availability of choice can pose challenges as well as provide benefits because when people have choices they must also make decisions. Appraising the likely results of different courses of action can sometimes be practically difficult and, where the likely impact of different possible outcomes is high, this may pose psychological strains on those presented with different options. This can give rise to what is sometimes called the 'burden of choice'. Making prenatal tests available to women and couples does not mean that they have to accept them, but it does oblige women and couples to make decisions about whether to accept or decline the offer. In the case of reproductive choice, women might find it difficult to make decisions either about whether to undergo prenatal testing or about how to proceed if a fetal anomaly is detected.¹³⁶ Decisions to terminate a pregnancy are also frequently described by pregnant women and couples as painful and distressing and the psychological impacts of having to make these choices can be significant (see Paragraph 1.17).
- 1.65 Even though a fetus does not have the same legal status as a child or adult, and there is disagreement about the moral status of the fetus (see Paragraph 1.49), a fetus has the potential to become a person capable of making autonomous choices in the future,

¹³⁴ The Abortion Act places constraints on reproductive autonomy (see Paragraph 1.49) and there is debate about the extent and nature of fetal information to which women and couples must have access in order to be in a position to exercise reproductive autonomy, given differing views on the interests or status of the fetus.

¹³⁵ According to Beauchamp and Childress: "...personal autonomy encompasses, at a minimum, self-rule that is free from both controlling interference by others and from certain limitations such as inadequate understanding that prevents meaningful choice." (Beauchamp TL and Childress JF (2001) *Principles of biomedical ethics* (Oxford: Oxford University Press)).

¹³⁶ See, for example Donovan S (2006) Inescapable burden of choice? The impact of a culture of prenatal screening on women's experiences of pregnancy *Health Sociology Review* **15**: 397-405.

and this might deserve recognition and respect. It is also sometimes said that the fetus has a *right to an open future* which might work as a ‘right in trust’ to exercise the autonomy of the person the fetus becomes will have.¹³⁷ Depending on what is being tested for, a parental decision to access NIPT could undermine the ability of the future person to make their own choices about accessing genetic information that might tell them about their future health, abilities, personality or physical attributes, or might violate ‘in advance’ a future person’s right to autonomy.

Avoidance of harm

- 1.66 Considerations relating to harm are important when appraising any novel healthcare intervention, including NIPT. All such developments pose potential risks of physical, psychological and broader societal harms that are important to take into account when assessing the possible impacts of any new healthcare technology.
- 1.67 The state has a role to play in eliminating, reducing or mitigating harms posed both by healthcare technologies or the interventions it makes available to people as part of publicly funded health care services, and by those that are commercially available to consumers in the private sector. This is an instance of a wider state duty to protect citizens from harm. Political liberalist John Stuart Mill’s view that “...the only purpose for which power can be rightfully exercised over any member of a civilized community, against his will, is to prevent harm to others”¹³⁸ has been influential in the modern politics of the Western world.¹³⁹ There are different ways of formulating liberal principles that take into account a harm principle like Mill’s, but all sanction some level of state intervention to constrain free choices in cases where unrestrained free actions might otherwise give rise to significant harms. In the context of NIPT, restricting freedoms in order to prevent harm to others may mean limiting the freedom to access NIPT in some circumstances in order to protect the fetus, or to prevent harm to wider society. Objectives to prevent harm may also extend to approaches that restrict an individual’s choices in order to prevent harm to that same individual. In the context of NIPT this might mean restricting access to NIPT in order to protect women from coming to harm.
- 1.68 Legislation, regulation and policy might be used by governments to limit or control access to, or in some cases prohibit, certain activities, products or services in order to minimise or reduce physical or psychological harm to different parties. Regulations prohibiting the sale of pharmaceutical drugs whose effects on human health are unknown, or food that does not meet health and safety standards are uncontroversial examples of the state constraining choices in order to minimise harm. Most accept that such interventions, in at least some instances, are warranted. In addition to restricting access to things that are unsafe, the state may impose requirements on providers of goods and services, such as providing accurate descriptions of their products to consumers, in order that the consumer is not exposed to psychological or financial harm, and can make an informed

¹³⁷ See, for example Feinberg J (1980) The child’s right to an open future, in *Whose child? Children’s rights, parental authority and state power*, Aiken W and LaFollette H (Editors) (US: Rowman and Littlefield) and Davis DS (1997) Genetic dilemmas and the child’s right to an open future *Hastings Center Report* 27: 7-15.

¹³⁸ Mill JS (1869) *On liberty* (UK: Longmans, Green, Reader, and Dyer).

¹³⁹ Adoption of a harm principle leaves a number of further substantive issues open. The harm principle, on its own, says nothing about what counts as a harm, or what harm is constituted by, or how to individuate ‘others’; see for example: Bradley B (2012) Doing away with harm *Philosophy and Phenomenological Research* 85: 390-412. Further, there are questions about instances of wrongdoing that may not involve direct harm; see for example: Stewart H (2010) The limits of the harm principle *Criminal Law and Philosophy* 4: 17-35. Nevertheless, the notion of harm reduction or avoidance has been influential in politics and policy and demonstrating evidence of harm, or risk of harm, is considered to be important in many areas of evidence based policy making.

choice about what risks she or he is willing to take to access the goods and services. The state also has a duty to consider broader, societal harms, which we discuss in Paragraphs 1.71-1.82.

- 1.69 The state has responsibilities to ensure that its own public healthcare services are safe and effective, and do not cause unnecessary harm to patients. This means that, where costs are neutral, governments should provide, within publicly funded healthcare services, treatments and tests that are safer, more efficacious and are associated with less discomfort or other negative side effects than alternative treatments and tests.
- 1.70 The avoidance of harm is also an important notion within healthcare and medical ethics. Doctors, nurses and other healthcare professionals are required to provide tests and treatments that are safe.¹⁴⁰

Equality, fairness and inclusion

- 1.71 The increasing availability and use of NIPT may be seen to undermine important societal values, such as equality, and the importance of cultivating a fair and inclusive society. Some uses of NIPT may be regarded as wrong if they lead to an increase in inequality, unfairness or social exclusion. In part, these concerns relate to the harms to which inequality could give rise for particular groups, as existing problems may be exacerbated. But importantly, the ethical concerns are also about the very principles at stake, and the extent to which NIPT can be used to support, rather than undermine, society's values of fairness, equality and inclusion.
- 1.72 Whilst different political models accord differing levels of priority to the value of equality, and there is disagreement about what equality consists in or how it should be realised,¹⁴¹ many agree that the aspiration to cultivate a fair and inclusive environment is an important objective in any society. In the context of a liberal state, some view inequalities as wrong in principle, in addition to having concerns about the harms to which those inequalities give rise. Many accept that the state has a role to play in addressing and minimising inequality and injustice, and has duties to promote equality and endeavour to ensure that all people are treated fairly and are not excluded from society.¹⁴²
- 1.73 Respecting the equal value of all people can involve enshrining principles of equality in law, in order that all members of society have the same legal access to goods, services and opportunities. However, such legal protections do not on their own guarantee societal equality. Even in societies where all people have the same legal rights, inequalities and injustices often persist. This can be because laws are routinely broken when, for example, people are discriminated against, or because law alone is not sufficient to alter entrenched societal or cultural conventions, nor to address the legacy of previous injustices. Societal inequalities persist at the levels of income, wealth, education, health, gender, age and elsewhere, even when people have equal legal rights. Equality in society might also be undermined when others exercise free choices, putting these values in tension with each other.

¹⁴⁰ See, for example, General Medical Council (2013) *Good medical practice*, available at: http://www.gmc-uk.org/static/documents/content/GMP_.pdf.

¹⁴¹ For example, there are differences amongst those who believe that societies are equal when all members have access to the same opportunities, and others who believe that the requirements of equality are that goods and resources are shared equally amongst all members of society.

¹⁴² Libertarian perspectives, which typically depict freedom and property as of fundamental value, are sometimes presented as political models that attach limited importance to equality. However, some libertarian views, sometimes described as 'left-libertarian' models aim to make room for considerations of equality. See for example: Otsuka M (2003) *Libertarianism without inequality* (Oxford: Clarendon Press).

- 1.74 Arguably, state duties to promote equality, fairness and inclusion involve taking proactive steps to develop policies that address entrenched societal inequalities, which may arise from prejudice, bias and discrimination or from social and political structures that unfairly benefit or disadvantage certain groups. Such policies might aim at minimising health inequalities through public health programmes, or by counteracting explicit and implicit biases that exist amongst educational institutions or employers. They might also involve addressing negative public attitudes towards certain groups and proactively promoting diversity and inclusion.
- 1.75 The state ought to consider equality issues in the context of publicly funded health service provision.¹⁴³ The UK Government, for example, has legal duties to provide public services to all individuals, part of which involves ensuring that there is equal access to NHS care.¹⁴⁴ The state must also consider how policies affect the population as a whole and should give due attention to any unintended consequences including, for example, the possibility that health or other inequalities may be created or worsened by a given intervention. The Nuffield Council on Bioethics' 2007 report *Public health: ethical issues* stated that: "Because many interventions bring potential harms as well as benefits, and the potential for both benefits and harms may be unevenly distributed in the population, this question must be answered by assessing the overall balance between risks and benefits, and how these are distributed among different members of the population."¹⁴⁵ This might involve assessing and weighing the nature of the risks and benefits concerned, and how particular groups might be affected, as well as how risks and harms aggregate.
- 1.76 The state also has duties to allocate public resources proportionately and to ensure that public money is spent fairly. All state spending carries opportunity costs and it is appropriate for governments to consider any given health intervention in the context of wider national policy and public spending.
- 1.77 Societal trends over the last 50 years have seen significant developments in advancing the equal status of disabled people, and general levels of wellbeing amongst disabled people have increased markedly in this period. Disabled people in the UK now have more rights, typically have higher life expectancy and access to better medical and social care, and enjoy greater access to educational, health and other opportunities than in the past.¹⁴⁶ Research on the quality of life experienced by people with a range of disabilities suggests that disabled people often have high levels of wellbeing and report subjective quality of life that is as good as or better than that of non-disabled people.¹⁴⁷ Nevertheless, it is widely recognised that disabled people in the UK do not currently have

¹⁴³ The Public Sector Equality Duty requires that public bodies consider how their policies and decisions affect people who are protected by the Equality Act 2010.

¹⁴⁴ NHS England (2015) *Guidance for NHS commissioners on equality and health inequalities legal duties*, available at: <https://www.england.nhs.uk/wp-content/uploads/2015/12/hlth-inqual-guid-comms-dec15.pdf>.

¹⁴⁵ Nuffield Council on Bioethics (2007) *Public health: ethical issues*, available at: <http://nuffieldbioethics.org/wp-content/uploads/2014/07/Public-health-ethical-issues.pdf>.

¹⁴⁶ Scope (2014) *Better living, higher standards: improving the lives of disabled people by 2020*, available at: <http://www.scope.org.uk/Scope/media/Documents/Publication%20Directory/Scope-report-Better-living,-higher-standards.pdf>; Department for Education and Skills (2004) *Removing barriers to achievement: the Government's strategy for SEN*, available at: <http://webarchive.nationalarchives.gov.uk/20130401151715/http://education.gov.uk/publications/eorderingdownload/dfes%200117%20200mig1994.pdf>; British Institute of Learning Disabilities (2012) *BILD factsheet: older people with a learning disability*, available at: <http://www.bild.org.uk/information/ageingwell/background/>.

¹⁴⁷ Wasserman D, Wachbroit R and Bickenbach J (2005) *Quality of life and human difference: genetic testing, health care, and disability* (Cambridge: Cambridge University Press).

access to the same opportunities as those without disabilities and continue to be discriminated against, excluded and marginalised.¹⁴⁸

- 1.78 There has also been a fundamental shift in how disability is viewed and, since the 1980s, there has been a significant change in understandings of what disability consists in and how it arises. The social model of disability has been key in this development.¹⁴⁹ Impairment, according to the social model, is a biological or medical condition of the body, which may include the loss of a sensory or motor function or physiological limitation. Disability is generated by the societal environment in which people with impairments live, which includes the prejudice, oppression or discrimination experienced by people with physical impairments. Many would argue that the social model can be overstated.¹⁵⁰ There is now a widespread acceptance that social and environmental factors, in combination with physical impairment, give rise to disability.¹⁵¹
- 1.79 These changes have occurred alongside the articulation of certain views in bioethics on prenatal screening and termination on the grounds of fetal anomaly, that these kinds of interventions in pregnancy are problematic insofar as they express negative or offensive messages to disabled people (see Paragraphs 2.65-2.69).¹⁵² Some have gone further and argue that termination on the grounds of fetal anomaly, which is made possible by prenatal screening, is wrong insofar as it constitutes a form of discrimination and is comparable to sex selection and, were it possible, termination on the grounds of sexual orientation or race.¹⁵³ Prenatal screening has therefore been criticised by some as being in tension with broader societal trends that have focused on strengthening and defending the equal rights of disabled people and their inclusion in wider society.
- 1.80 On the other hand, enhanced reproductive choice is seen by some to play an important role in advancing gender equality.¹⁵⁴ The legalisation of abortion and the development of prenatal screening have enabled women to exercise greater control over the

¹⁴⁸ United Nations Committee on the Rights of Persons with Disabilities (2016) *Inquiry concerning the United Kingdom of Great Britain and Northern Ireland carried out by the Committee under article 6 of the Optional Protocol to the Convention on the Rights of Persons with Disabilities*, available at:

http://tbinternet.ohchr.org/_layouts/treatybodyexternal/TBSearch.aspx?Lang=en&TreatyID=4&DocTypeCategoryID=7; Scope (2014) *Better living, higher standards: improving the lives of disabled people by 2020*, available at:

<http://www.scope.org.uk/Scope/media/Documents/Publication%20Directory/Scope-report-Better-living,-higher-standards.pdf>

¹⁴⁹ There are a number of academic articulations of the social model of disability; see for example: Oliver M (1990) *The politics of disablement* (Basingstoke: Macmillan); Oliver M (1996) *Understanding disability: from theory to practice* (New York: St Martin's Press); Shakespeare TW (2006) *Disability rights and wrongs* (London: Routledge). The notion that social aspects are significant in giving rise to disability has also penetrated wider civil society and the charity Scope, for instance, says on its website: "The social model of disability says that disability is caused by the way society is organised, rather than by a person's impairment or difference. It looks at ways of removing barriers that restrict life choices for disabled people. When barriers are removed, disabled people can be independent and equal in society, with choice and control over their own lives" (Scope (2017) *The social model of disability*, available at: <http://www.scope.org.uk/about-us/our-brand/social-model-of-disability>).

¹⁵⁰ Shakespeare T (2014) *Disability rights and wrongs revisited* (London: Routledge).

¹⁵¹ World Health Organization (2002) *Towards a common language for functioning, disability and health. The international classification of functioning, disability and health*, available at:

<http://www.who.int/classifications/icf/training/icfbeginnersguide.pdf>.

¹⁵² Parens E and Asch A (2000) *Prenatal testing and disability rights* (Washington, DC: Georgetown University Press).

¹⁵³ Asch A (1999) Prenatal diagnosis and selective abortion: a challenge to practice and policy *American Journal of Public Health* 89: 1649-57.

¹⁵⁴ The fact that in many societies the responsibilities of parenthood fall disproportionately on women, with inevitable consequences for their freedom to pursue career, leisure and other goals, has been observed by a number of feminist writers. Ellen Willis, for example, has argued that: "We live in a society that defines childrearing as the mother's job; a society in which most women are denied access to work that pays enough to support a family, childcare facilities they can't afford, or any relief from the constant, daily burdens of motherhood.... Under these conditions the unwillingly pregnant woman faces a terrifying loss of control over her fate" (Willis E (1992) Abortion: is a woman a person?, in *Powers of desire: the politics of sexuality*, Snitow A, Stansell C and Thompson S (Editors) (New York: NYU Press) pp 471-476). See also, Saul JM (2003) *Feminism: Issues and arguments* (Oxford: Oxford University Press); Jaggar AM (1995) Abortion and a woman's right to decide, in *Women and philosophy: Toward a theory of liberation*, Gould CC and Wartofsky MW (Editors) (New York: Putnam's), pp 347-364.

circumstances under which they become mothers, which has the potential to impact in significant ways on their role and position in the workplace, and society more generally, given that in most societies many of the responsibilities of parenthood fall to women. There is also debate about whether the availability of new screening technologies may exert pressure on women to make use of them during pregnancy, and the wider impact of other forms of reproductive technology on gender issues includes discussion of both negative and positive potential consequences for women.¹⁵⁵ One consequence of the availability of prenatal screening is that women are, in practice, now often able to defer parenthood to some extent, if they choose, and this has gone some way towards enabling more women to make choices to combine pregnancy and motherhood with professional and other aspects of their lives, should they want to, in ways that best suit them.

- 1.81 More recent trends in the UK towards women becoming mothers later in life are particularly relevant when considering the potential impacts of NIPT.¹⁵⁶ For women who want to become mothers later, the availability of safe and accurate prenatal testing for conditions associated with advanced maternal age, such as Down's, Edwards' and Patau's syndromes, might help them to pursue other life opportunities without needing to accept the higher chance of giving birth to a child with a genetic condition or variation, should they wish to avoid this.
- 1.82 Currently, NIPT is mostly available only to those who can afford to pay for it in the private sector. This means that there is potential for health inequalities to be created or worsened by the fact that the goods of NIPT are, at the moment, inaccessible to those with less financial means. It might be thought unfair that those who are already better off financially may benefit exclusively from the enhanced choice that NIPT can provide.
- 1.83 Healthcare professionals also have duties to treat patients fairly and consistently within healthcare settings. Healthcare professionals and those working in health management have parallel responsibilities to those held by the state to its citizens to treat each patient fairly, and to ensure that similarly situated patients are treated similarly.¹⁵⁷

¹⁵⁵ Widdows H (2009) The Janus-face of new reproductive technologies: escaping the polarised debate *International Journal of Public Theology* 4: 76–99 .

¹⁵⁶ Office for National Statistics (2016) *Births in England and Wales: 2015*, available at: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthsummarytablesenglandandwales/2015>.

¹⁵⁷ Beauchamp TL and Childress JF (2001) *Principles of biomedical ethics* (Oxford: Oxford University Press).

Chapter 2

NIPT in NHS prenatal screening for Down's, Edwards' and Patau's syndromes

Chapter 2 - NIPT in NHS screening for Down's, Edwards' and Patau's syndromes

Chapter overview

From 2018, pregnant women who are found to have at least a 1 in 150 chance of their fetus having Down's, Edwards' or Patau's syndromes after having the 'combined' screening test will be offered non-invasive prenatal testing (NIPT) as a second stage screening test in the NHS. Research suggests that this will increase prenatal diagnoses, giving more women the opportunity to prepare for a disabled child or to have a termination, and will lower the number of invasive diagnostic tests, reducing procedure-related miscarriages.

It might be thought unfair or inequitable that only some women will be offered NIPT in the NHS. However, offering NIPT to all pregnant women could lead to a higher number of false positive results and test failures, and therefore more invasive diagnostic procedures.

Offering NIPT as a second stage test may lead to a delay in diagnosis for some women, which may be significant to those considering a termination.

There are concerns that women and couples will think NIPT is equivalent to a diagnostic test, or that it is a 'routine' part of prenatal care. Some healthcare professionals may be focusing on medical problems when imparting information about Down's syndrome, without describing more fully what it can be like to have a child with Down's syndrome. Non-NHS sources of advice, the presentation of disability and prenatal testing in the media, and the perceived impact of a disabled child on the family may also influence the decisions women and couples make. The provision of accurate, balanced information that supports all screening choices equally and the need for sufficient time to discuss any concerns are essential requirements of the introduction of NIPT in the NHS.

Introducing NIPT in the NHS could lead to an increase in the number of terminations following a diagnosis of Down's, Edwards' or Patau's syndromes. Some believe this amounts to eugenics. If this leads to a significant reduction in the number of people born and living with these syndromes, it is possible that the quality of health and social care they receive and the importance attributed to research into these syndromes will be affected. Making NIPT available in the NHS could be perceived as sending negative and hurtful messages about the value of people with the syndromes being tested for.

The introduction of NIPT may lead to changes in demand for related NHS services such as genetic counselling, invasive diagnostic testing, termination and laboratory services. There are no national standards or guidelines on antenatal care for women who choose to continue their pregnancy after a diagnosis of a fetal anomaly.

NIPT for other genetic conditions or impairments could be proposed for inclusion in NHS prenatal screening programmes in the future. Recognising that there may be wider consequences of prenatal screening, beyond those being aimed for, is important for the appraisal of the appropriateness of screening programmes.

Introduction

- 2.1 Screening is the process of identifying people who may have an increased chance of having a condition. The NHS runs several antenatal and newborn screening programmes, including the fetal anomaly screening programme (FASP), which offers screening to pregnant women for Down's, Edwards' and Patau's syndromes and fetal anomalies. In January 2016, the UK National Screening Committee (UKNSC) recommended an 'evaluative implementation' of non-invasive prenatal screening (NIPT) for Down's, Edwards' and Patau's syndromes in the NHS fetal anomaly screening programme. In November 2016, the Department of Health agreed to implement the UKNSC's recommendation and offer NIPT in the NHS. From some point in 2018, pregnant women who are found to have at least a 1 in 150 (0.67 per cent) chance of their fetus having Down's, Edwards' or Patau's syndromes after having the combined test will be offered NIPT or an invasive diagnostic test by their NHS care provider. Those who choose NIPT and get a high chance result will be offered invasive diagnostic testing to get a definitive diagnosis. The UKNSC recommended an evaluative implementation process to better understand how NIPT will perform in an NHS screening programme pathway before full implementation within the NHS.¹⁵⁸
- 2.2 This chapter considers the potential implications for different parties of offering NIPT as a second stage test in the NHS prenatal screening programme. The fact that prenatal screening for Down's, Edwards' and Patau's syndromes is already offered in the NHS is taken as a starting point, and the way in which screening is offered now and in future is examined. At the end of the chapter, we make some observations regarding the way in which decisions about national prenatal screening programmes are made, and how they are reviewed and evaluated, given that it is possible that more genetic conditions will become candidates for future prenatal screening programmes involving NIPT that will need assessment by the UKNSC.

Pilot studies: NIPT in NHS screening

- 2.3 A key part of the evidence that informed the UKNSC's recommendation was the Reliable, Accurate Prenatal, non-Invasive Diagnosis (RAPID) research programme, funded by the National Institute for Health Research (NIHR). The study examined: how NIPT might best be utilised in the NHS Down's syndrome screening pathway; test performance; the acceptability of NIPT to women and healthcare professionals; the benefits and costs of NIPT; and the implications for implementing NIPT at a population level.¹⁵⁹
- 2.4 The study took place in eight NHS hospitals between November 2013 and February 2015. The study researchers trained local midwives, and all pregnant women were sent information on NIPT with their booking information. Pregnant women who were found to have at least a 1 in 1000 (0.01 per cent) chance of having a fetus with Down's syndrome following the combined screening test were given more detailed information and the opportunity to discuss NIPT with a healthcare professional. Women who had at least a 1 in 150 (0.67 per cent) chance of having a fetus with Down's syndrome were offered NIPT, invasive diagnostic testing or no further testing. Pregnant women who were found

¹⁵⁸ UK National Screening Committee (2016) *UK NSC non-invasive prenatal testing (NIPT) recommendation*, available at: https://legacyscreening.phe.org.uk/policydb_download.php?doc=570.

¹⁵⁹ Chitty LS, Wright D, Hill M *et al.* (2016) Uptake, outcomes, and costs of implementing non-invasive prenatal testing for Down's syndrome into NHS maternity care: prospective cohort study in eight diverse maternity units *British Medical Journal* **354**: i3426.

to have between a 1 in 151 (0.67 per cent) and a 1 in 1000 (0.1 per cent) chance of having a fetus with Down's syndrome were offered NIPT or no further testing. Women who were offered NIPT were given information about the test and were offered an appointment with a healthcare professional who had been trained by the study researchers. Of the women who chose to have NIPT, testing for Down's, Edwards' and Patau's syndromes was carried out.

- 2.5 In total, 30,790 women opted for screening at the hospitals involved in the study. Following the combined test, 934 women were found to have at least a 1 in 150 (0.67 per cent) chance of having a fetus with Down's syndrome. Of those women, 695 (75 per cent) accepted NIPT, 166 (18 per cent) opted to go directly to invasive diagnostic testing and 73 (8 per cent) declined any further testing. Uptake of follow-up testing (NIPT or invasive diagnostic testing) among the women in the study was 93 per cent. Before NIPT was available, uptake of follow-up invasive diagnostic testing was 54 per cent in the study centres. NIPT was also offered to women who were found to have between a 1 in 150 (0.67 per cent) and a 1 in 1000 (0.1 per cent) chance of having a fetus with Down's syndrome.
- 2.6 In total, 2,493 women accepted NIPT in the study (which included women in both the high and medium chance categories). Of these, 59 (2 per cent) received a result that their fetuses were 'highly likely to be affected' by Down's, Edwards' or Patau's syndromes. Two of these women had miscarriages. The decisions made by the remaining women are outlined below:
 - Of the 57 women who received a result of 'highly likely to be affected', 47 (82 per cent) accepted invasive diagnostic testing and ten (18 per cent) declined any further testing.
 - Of the 47 women who had invasive diagnostic testing, the NIPT result was found to be false in five of the women (11 per cent) and a chromosome anomaly was confirmed in the fetuses of 42 women (89 per cent). Among the women with a confirmed anomaly, 35 (83 per cent) had a termination (29 fetuses had Down's syndrome, four had Edwards' syndrome and two had another chromosome anomaly) and seven (17 per cent) continued with their pregnancy. Three of these had miscarriages (two fetuses with Down's syndrome and one with Edwards' syndrome) and four had live births (all with Down's syndrome).
 - Of the ten women who declined further testing after NIPT, two (20 per cent) had a termination (one had a fetus with Down's syndrome and one had a fetus with Edwards' syndrome) and the other eight (80 per cent) elected to continue, leading to six live births (all had Down's syndrome), one stillbirth (Down's syndrome) and one neonatal death (Patau's syndrome).
 - In summary, of the 52 women who either had a fetus with a confirmed diagnosis from invasive testing or had a high chance NIPT result and decided not to have further investigation, 37 (71 per cent) decided to terminate their pregnancy and 15 (29 per cent) decided to continue. Ten babies were born alive, all of whom had Down's syndrome. Five babies miscarried, were stillborn or died shortly after birth.
- 2.7 The authors used their results to estimate the costs and consequences of introducing NIPT into current Down's syndrome screening across the UK. They predicted that offering NIPT to women who are found to have at least a 1 in 150 (0.67 per cent) chance of having a fetus with Down's syndrome following the combined test, with the option of going direct to invasive diagnostic testing, would result in:

- 195 more fetuses with Down's syndrome being identified per year;
- 3368 fewer invasive diagnostic tests being carried out;
- 17 fewer procedure-related miscarriages; and
- a slight reduction in the cost of the screening programme.

These figures are based on assumptions about the number of women who will get pregnant each year, the number of women who will opt for screening and follow-up testing, and the cost of NIPT. The rate of miscarriage following amniocentesis and chorionic villus sampling (CVS) is assumed to be 0.5 per cent but, as previously discussed, this is contested (see Paragraph 1.10). The RAPID study did not include twin or multiple pregnancies.

- 2.8 Another study considered the implications of introducing NIPT into the NHS prenatal screening programme at two hospitals in England between October 2013 and February 2015. Of the 460 women who were found to have at least a 1 in 100 (1 per cent) chance of having a fetus with Down's syndrome following the combined screening test at 10-13 weeks, 276 (60 per cent) accepted NIPT, 173 (38 per cent) opted to go directly to invasive diagnostic testing and eleven (2 per cent) declined any further testing. The authors estimate that the introduction of NIPT was associated with a 43 per cent reduction in the rate of invasive testing.¹⁶⁰

Implications of introducing NIPT in NHS prenatal screening

Test safety and performance

- 2.9 Evidence shows that NIPT is a safe and accurate prenatal test for predicting Down's syndrome. The RAPID study suggests that offering NIPT to women who are found to have at least a 1 in 150 (0.67 per cent) chance of having a fetus with Down's syndrome would increase the number of fetuses with Down's syndrome identified in the screening programme. NIPT has been shown to be a slightly less accurate test for predicting Edwards' and Patau's syndromes, but it is more accurate than the combined test for detecting these syndromes. In addition, NIPT is associated with fewer false positive results than the combined test. When NIPT is available to women following a high-chance result from the combined test, it is likely that fewer women will proceed to invasive diagnostic testing, reducing the number of procedure-related miscarriages that occur. This combination of accuracy and safety has the potential to reduce anxiety during pregnancy, such as among women who would not have a diagnostic invasive test. Several respondents to our survey highlighted accuracy and safety as benefits of introducing NIPT into the NHS.

"It will give them access to more advanced and sensitive screening." (Researcher – survey respondent)

"For those who would have considered invasive testing, there is a lower risk option to reduce the number of women needing invasive tests, reducing the number of pregnancies compromised." (Person with experience of undergoing NIPT – survey respondent)

¹⁶⁰ Gil M, Revello R, Poon L, Akolekar R and Nicolaides K (2016) Clinical implementation of routine screening for fetal trisomies in the UK NHS: cell-free DNA test contingent on results from first-trimester combined test *Ultrasound in Obstetrics & Gynecology* 47: 45-52.

2.10 NIPT can result in test failure, when no results are produced, and inconclusive or indeterminate results, when the result is in a middle-range which is neither positive nor negative (see Paragraph 1.20). The American College of Medical Genetics and Genomics (ACMG) recommends offering diagnostic testing to women who have had a 'no call' result if the test was carried out at an appropriate gestational age; offering a repeat NIPT test is not recommended.¹⁶¹ In the RAPID study, women with inconclusive or failed tests were offered repeat NIPT. Those who had at least a 1 in 150 (0.67 per cent) chance of having a fetus with Down's syndrome, as determined by the combined test, were offered the choice of invasive testing as well. Failed or inconclusive tests may prolong the screening pathway for some women and may result in greater anxiety. It is essential that the chances of a false positive result and the possibility of failed or inconclusive tests are clearly communicated to pregnant women and couples who are offered NIPT. The RAPID study did not include twin or multiple pregnancies and so further research is needed before NIPT is offered to women with twins/multiples in the NHS.

Access

2.11 The devolved governments have all declared a duty to reduce inequalities in health and have recognised the need to reduce inequalities in access to healthcare services.¹⁶² The Working Group believes that prenatal screening constitutes a healthcare service, given that it can enable pregnant women to make informed choices during pregnancy and potentially access other healthcare services, such as specialist antenatal care or abortion services. Currently, NIPT is only available as a paid-for service in the private sector and for free in a few NHS hospitals (mainly those that were involved in the RAPID study and continued to offer NIPT after the study ended). Introducing NIPT into the NHS prenatal screening pathway as a second stage test would mean that any pregnant woman in the UK with at least a 1 in 150 (0.67 per cent) chance that her fetus has Down's, Edwards' or Patau's syndrome will be able to access NIPT if they choose. As a result of accepting the offer of screening, those women who choose to do so can potentially access other healthcare services, such as specialist antenatal care or termination services. Therefore, the Working Group believes that offering NIPT within the NHS screening pathway to women with a higher chance combined test result will reduce inequalities in access to healthcare services.

2.12 However, some believe that offering NIPT only to women who receive a high chance result following the combined test is still unfair or inequitable. Only approximately three per cent of pregnant women who opt for screening will fall into this category.¹⁶³ Of the women who receive lower chance results following the combined test, a proportion

¹⁶¹ Gregg AR, Skotko BG, Benkendorf JL *et al.* (2016) Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics *Genetics in Medicine* **18**: 1056-65.

¹⁶² NHS England (2015) *Guidance for NHS commissioners on equality and health inequalities legal duties*, available at: <https://www.england.nhs.uk/wp-content/uploads/2015/12/hlth-inqual-guid-comms-dec15.pdf>; PHE England (2016) *About us*, available at: <https://www.gov.uk/government/organisations/public-health-england/about>; Public Health Wales (2015) *Creating a healthier, happier and fairer Wales for everyone. Introducing the Public Health Wales strategic plan for 2015-18*, available at: <http://www.wales.nhs.uk/sitesplus/documents/888/PHW%20Introducing%20the%20strategic%20plan%20booklet%20E.pdf>; Northern Ireland Executive (2014) *Making life better. A whole system strategic framework for public health 2013-2023*, available at: https://www.health-ni.gov.uk/sites/default/files/publications/dhssps/making-life-better-strategic-framework-2013-2023_0.pdf; The Scottish Government (2010) *The healthcare quality strategy for NHS Scotland*, available at: <http://www.gov.scot/resource/doc/311667/0098354.pdf>.

¹⁶³ Public Health England (2016) *NHS screening programmes in England 1 April 2015 to 31 March 2016*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/574713/Screening_in_England_2015_to_2016.pdf.

(approximately 16 per cent according to some studies)¹⁶⁴ will receive a false negative result from the combined test. These women will be told that they have a low chance of having a fetus with Down's, Edwards' or Patau's syndrome, when in fact the fetus is affected. Down's, Edwards' or Patau's syndrome may be picked up at ultrasound scans later in pregnancy, but for many an earlier diagnosis would be preferable. It could be argued that if all pregnant women were offered NIPT, given that NIPT returns fewer false positive results than the combined test, some of these women would not receive a false negative result and would receive their diagnosis earlier. However, a small proportion of women who have NIPT as a first tier test will also receive a false negative result.¹⁶⁵ It is not known whether the same women with a false negative result from the combined test would also receive a false negative result from NIPT. One of the implications of the recent *Montgomery v. Lanarkshire Health Board* UK Supreme Court decision might be that healthcare professionals are now obliged to inform women and couples who are not eligible for NIPT in the NHS about the availability of NIPT in the private sector as a 'reasonable alternative'.

- 2.13 The Working Group is sensitive to ethical issues relating to access, equality and fairness when new healthcare technologies become available. However, we do not believe that there is any automatic imperative to make a treatment or test available to everyone on the NHS on the grounds of equal access just because it is available in the private sector. There also must be evidence of benefit to those to whom it is offered and that providing the test would be a fair and proportionate use of public resources. NIPT for Down's syndrome has a lower positive predictive value when used by the general population of pregnant women, compared to when it is used by women with a higher chance of their fetuses having the condition (see Box 1.3, p13). In addition, test failure would be a problem if NIPT was offered to all pregnant women, as even a seemingly small test failure rate of 2.5 per cent would lead to high numbers of women not receiving any results and potentially being offered an invasive test.¹⁶⁶ The Warwick Evidence review of NIPT estimated that offering NIPT as a first stage screening test to all pregnant women would result in over 13,000 initial test failures, whereas it is estimated that offering it as a second stage screening test following the combined test would result in 385 initial test failures.¹⁶⁷
- 2.14 The findings of the RAPID study provide further indication of the implications of offering NIPT to pregnant women in lower chance categories. The study authors estimate that if women with a 1 in 500 (0.2 per cent) chance of having a fetus with Down's syndrome were offered NIPT, this would lead to 237 more fetuses with Down's syndrome being identified per year, 3,334 fewer invasive diagnostic procedures being carried out, and 17 fewer procedure-related miscarriages, and would cost approximately an additional £3 million per year. If women with a 1 in 1000 (0.1 per cent) chance of having a fetus with Down's syndrome were offered NIPT, it is estimated that this would lead to 256 more fetuses with Down's syndrome being identified per year, 3,319 fewer invasive diagnostic

¹⁶⁴ Taylor-Phillips S, Freeman K, Geppert J et al. (2015) *Systematic review and cost-consequence assessment of cell-free DNA testing for T21, T18 and T13 in the UK – final report*, available at: https://legacyscreening.phe.org.uk/policydb_download.php?doc=552.

¹⁶⁵ The Warwick review suggested the probability of a false negative result with NIPT for Down's syndrome in the general obstetric population is 1 in 5570, or 0.02 per cent: Taylor-Phillips S, Freeman K, Geppert J et al. (2016) Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis *BMJ Open* 6: e010002.

¹⁶⁶ Wald NJ and Bestwick JP (2015) Performance of antenatal reflex DNA screening for Down's syndrome *Journal of Medical Screening* 22: 168-74.

¹⁶⁷ Taylor-Phillips S, Freeman K, Geppert J et al. (2015) *Systematic review and cost-consequence assessment of cell-free DNA testing for T21, T18 and T13 in the UK – final report*, available at: https://legacyscreening.phe.org.uk/policydb_download.php?doc=552.

procedures being carried out and 17 fewer procedure-related miscarriages, and would cost approximately an additional £7 million per year.¹⁶⁸ Compared to the predicted implications of offering NIPT to women with a 1 in 150 (0.67 per cent) chance of having a fetus with Down's syndrome, offering NIPT to women in the lower chance categories is predicted to increase slightly the number of fetuses with Down's syndrome detected, not to change the number of procedure-related miscarriages and to be significantly more costly (see Paragraph 2.7). This raises questions about whether such an increase in the use of state resources would be proportionate to the resulting promotion of choice and reduction in harm.

- 2.15 A further concern relating to offering NIPT only to women after they have had the combined test is that it may lead to a delay in diagnosis for some women. The combined test takes place at between 10 and 14 weeks of pregnancy and the aim is for results to be returned within three working days.¹⁶⁹ Currently, women who are estimated to have at least a 1 in 150 (0.67 per cent) chance of having a fetus with Down's, Edwards' or Patau's syndromes are offered a diagnostic test (CVS or amniocentesis). If NIPT is offered to these women first and they accept, it is likely to take at least a week for NIPT to be carried out and for the results to be returned. Women with a high chance result following NIPT will still need to have a diagnostic test if they want a definitive diagnosis. This delay of a week or longer will be significant to some women, particularly those considering a termination. Some research suggests that later terminations are associated with higher levels of stress for women than first trimester terminations, at least in the short term.¹⁷⁰ A delay in diagnosis therefore, could be viewed as increasing harm to the pregnant woman in cases when a termination is being considered. It will be important that women are able to go straight to diagnostic testing after a high chance combined test result if they wish.

Provision of information and support

- 2.16 In theory, the only change to the information and support provided to women and couples following the introduction of NIPT to the NHS screening programme should be the addition of explanations of how NIPT works and the interpretation of results. However, concerns were raised by respondents to our survey and consultation about the quality of information and support currently provided to or accessed by women and couples undergoing prenatal screening. These concerns relate to challenges to ensuring women and couples are making informed, autonomous choices, and these challenges may be intensified by the introduction of NIPT. On the other hand, the introduction of NIPT may provide new opportunities to talk about Down's syndrome with women and couples when discussing screening with them.

Existing standards, guidance and law

- 2.17 NHS service specifications outline service and quality indicators for commissioners and providers of screening services. For example, NHS England Service Specification 16 covers prenatal screening for Down's, Edwards' and Patau's syndromes and sets out the

¹⁶⁸ Chitty LS, Wright D, Hill M *et al.* (2016) Uptake, outcomes, and costs of implementing non-invasive prenatal testing for Down's syndrome into NHS maternity care: prospective cohort study in eight diverse maternity units *British Medical Journal* **354**: i3426.

¹⁶⁹ Public Health England (2015) *Fetal anomaly screening programme standards 2015-16*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/421650/FASP_Standards_April_2015_final_2_.pdf.

¹⁷⁰ Daugirdaitė V, van den Akker O and Purewal S (2015) Posttraumatic stress and posttraumatic stress disorder after termination of pregnancy and reproductive loss: a systematic review *Journal of Pregnancy* **2015**: 646345.

care pathway that pregnant women should expect and how that service should be delivered. It states that during the first contact or booking visit with the midwife, verbal and written information about screening (using the NHS booklet *Screening tests for you and your baby*)¹⁷¹ should be given to the woman to enable her to make informed choices. If a woman has screening and diagnostic testing and receives a positive result, the woman should be “given the opportunity to discuss the results with health professionals who are knowledgeable about Down's, Edwards' and Patau's syndromes. This will include the offer of a termination of pregnancy or continuing support through pregnancy.” It is not stated who the health professionals should be or what kind of knowledge they should have. Screening providers must monitor and report on how they have delivered these specifications against set performance indicators.¹⁷² The NHS Scotland National Protocol for Fetal Anomaly and Down's syndrome screening requires that screening should be discussed as an ‘option’ rather than an inevitable aspect of routine maternity care. Women and their partners should be provided with information including: the implications of receiving a high or low chance result; information on the false positive rates of the screening test; the techniques involved and risks that may be associated with any diagnostic tests and also information about the conditions themselves.¹⁷³ NHS Scotland has produced the booklet *Your guide to screening tests during pregnancy*.¹⁷⁴

- 2.18 National Institute for Health and Care Excellence (NICE) Clinical Guidance on antenatal care for uncomplicated pregnancies (which applies in England) states that women should understand that it is their choice whether or not to embark on screening and that information about screening should be given to pregnant women at the first contact with a healthcare professional. This information should include the decisions that need to be made at each point along the pathway and their consequences, together with balanced and accurate information about Down's, Edwards' and Patau's syndromes. If a pregnant woman receives a high chance screening result, the guidance states that she should have rapid access to appropriate counselling by trained staff.¹⁷⁵
- 2.19 The Royal College of Obstetricians and Gynaecologists (RCOG) explanatory guidance for its members on termination for fetal anomaly includes advice on the information and support that should be provided to women and couples following a diagnosis of fetal anomaly. The guidance recognises that women and their partners will need as much information as possible on the implications of the diagnosis. It suggests that obstetricians are not always best placed to advise on outcomes after birth and, in some situations, input from other medical specialists, such as paediatricians, paediatric surgeons, geneticists and neonatologists, may be required to ensure a more comprehensive and balanced approach. All staff involved in the care of a woman or couple facing a possible termination of pregnancy are advised to adopt a non-directive, non-judgmental and supportive approach. There is no separate RCOG guidance on continuing pregnancy

¹⁷¹ Public Health England (2016) *Screening tests for you and your baby*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/529950/STFYAYB_May_2016_for_website.pdf

¹⁷² NHS England (2016) *Service Specification no. 16. NHS Fetal anomaly screening programme - screening for Down's, Edwards' and Patau's Syndromes (trisomy 21, 18 & 13)*, available at: <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/04/serv-spec-16-apr16.pdf>.

¹⁷³ NHS Scotland (2015) *National protocols: fetal anomaly and Down's syndrome screening* available at: <http://www.nsd.scot.nhs.uk/Documents/2015%20-%20Fetal%20Anomaly%20and%20Down's%20Syndrome%20Screening%20Protocols%20-%20v%201.pdf>.

¹⁷⁴ NHS Health Scotland (2016) *Your guide to screening tests during pregnancy: 2016 edition*, available at: <http://www.healthscotland.com/uploads/documents/3985-Your%20Guide%20To%20Screening%20Tests%20During%20Pregnancy-English-05-16.pdf>.

¹⁷⁵ The National Institute for Health and Care Excellence (2016) *Antenatal care for uncomplicated pregnancies. Clinical guidance CG62*, available at: <https://www.nice.org.uk/guidance/cg62>.

after diagnosis of fetal anomaly. The guidance on termination includes a section on this however, and states that a decision by a woman to continue her pregnancy must be fully supported and it should not be assumed that, even in the presence of an obviously fatal fetal condition, a woman will choose to have a termination. Members are advised that it can be helpful to use appropriate literature and the help of external agencies, such as Antenatal Results and Choices (see Paragraph 2.33).¹⁷⁶

- 2.20 Also relevant in this context is the recent decision of the UK Supreme Court in *Montgomery v. Lanarkshire Health Board*. A reasonable reading of the judgment assumes that at all stages of pregnancy a woman has a right to be informed about the options that are available to her and to be informed about the risks and consequences of any tests or treatment options, which might include NIPT (see Paragraph 1.45).¹⁷⁷

Verbal information and support

- 2.21 Many respondents to our survey and consultation (see Appendix: Method of working) believed the information and support that is provided by NHS healthcare professionals to pregnant women during the current screening process to be of a high standard.¹⁷⁸

"My personal experience was good; I received up-to-date and accurate information in a timely manner." (Person with multiple interests in NIPT – survey respondent¹⁷⁹)

"We felt informed, confident and supported by the staff we dealt with." (Person with multiple interests in NIPT – survey respondent¹⁸⁰)

- 2.22 However, research has shown that healthcare professionals involved in screening can have difficulty in communicating information about Down's, Edwards' and Patau's syndromes in a way that appears to support all options equally. This is thought to stem from a range of factors, including the lack of time that is available to discuss screening with women, the challenge of conveying complex information, language barriers and a lack of knowledge about Down's syndrome.¹⁸¹ This was supported by some of the concerns raised by respondents to our survey and consultation. In particular, the verbal information about Down's syndrome being given by healthcare professionals to pregnant women and couples, particularly after a diagnosis of fetal anomaly, was heavily criticised by the families of people with Down's syndrome who we heard from. There was concern that healthcare professionals, when imparting information following a diagnosis, tend to focus on the medical problems associated with the condition, such as heart problems,

¹⁷⁶ Royal College of Obstetricians and Gynaecologists (2010) *Termination of pregnancy for fetal abnormality in England, Wales and Scotland*, available at: <https://www.rcog.org.uk/globalassets/documents/guidelines/terminationpregnancyreport18may2010.pdf>.

¹⁷⁷ Brownsword R and Wale J (2016) The development of non-invasive prenatal testing: some legal and ethical questions *Annual Review of Law and Ethics* **24**.

¹⁷⁸ We did not systematically collect information from respondents to our survey about their personal experiences of receiving screening test results, so we cannot be sure that the responses came from people who had a range of outcomes.

¹⁷⁹ Survey respondent with recent experience of being pregnant, a general professional interest in prenatal testing, a family member or close friend with a genetic condition and a general interest in prenatal testing.

¹⁸⁰ Survey respondent with experience of undergoing NIPT and a family member or close friend with a genetic condition.

¹⁸¹ Barr O and Skirton H (2013) Informed decision making regarding antenatal screening for fetal abnormality in the United Kingdom: a qualitative study of parents and professionals *Nursing and Health Science* **15**: 318-25; Sooben RD (2010) Antenatal testing and the subsequent birth of a child with Down syndrome: a phenomenological study of parents' experiences *Journal of Intellectual Disabilities* **14**: 79-94; Williams C, Alderson P and Farsides B (2002) Dilemmas encountered by health practitioners offering nuchal translucency screening: a qualitative case study *Prenatal diagnosis* **22**: 216-20; Garcia E, Timmermans DR and van Leeuwen E (2008) The impact of ethical beliefs on decisions about prenatal screening tests: searching for justification *Social Science and Medicine* **66**: 753-64; Ekelin M and Crang-Svalenius E (2004) Midwives' attitudes to and knowledge about a newly introduced foetal screening method *Scandinavian Journal of Caring Sciences* **18**: 287-93; Heyman B, Hundt G, Sandall J *et al.* (2006) On being at higher risk: a qualitative study of prenatal screening for chromosomal anomalies *Social Science and Medicine* **62**: 2360-72; Williams C, Alderson P and Farsides B (2002) What constitutes 'balanced' information in the practitioners' portrayals of Down's syndrome? *Midwifery* **18**: 230-7.

and learning disabilities, without describing fully the more social aspects of the condition. Information about the social aspects, we heard, can be the kind of information in which women with a prenatal diagnosis of Down's syndrome are particularly interested so as to help them answer questions such as: where will my child go to school? Will they be able to make friends? Will they be able to have a job? It was argued that, without a rounded picture of what life with a person with Down's syndrome may hold, an informed decision about whether to continue or terminate the pregnancy cannot take place. In addition, we heard anecdotally that Edwards' and Patau's syndromes are often presented only in light of the associated high rates of stillbirth and death in early infancy.

"I worry... that consultants talk of poor quality of life, severe disabilities, major health complications when actually most individuals with Down's syndrome lead fulfilling, healthy and happy lives." (Person with a family member or close friend with a genetic condition – survey respondent)

"We just live life to the fullest as much as we can. And we learn like everyone else but we take longer to get to the achievements." (Person with Down's syndrome – interviewee)

"The first thing people think of Down syndrome is it's sad and that it's scary. They don't know much about it." (Person with Down's syndrome – interviewee)

Pregnant women and couples should receive a balanced¹⁸² portrayal of what to expect following a diagnosis of Down's, Edwards' or Patau's syndrome, and how their child may be cared for after birth. Research has found that, when discussing a prenatal diagnosis, specialists typically gave parents a better idea of what to expect during pregnancy and after birth than non-specialist obstetricians and this helped them feel more confident, less uncertain and more secure with their care.¹⁸³

- 2.23 It is also essential that healthcare professionals have a high level of understanding about screening tests and NIPT, including the test benefits and limitations. Some respondents were concerned about how the accuracy of NIPT for detecting Down's, Edwards' and Patau's syndromes in fetuses will be communicated to pregnant women and couples. For example, the specificity and sensitivity of NIPT vary for different women and for different conditions, and there is a chance of receiving a false positive result (see Box 1.3, p13). Presenting NIPT as '99 per cent accurate', for example, might lead some women to believe it is equivalent to a diagnostic test, and potentially opt to have a termination without having a diagnostic test. Conveying the positive predictive value of a test is crucial in this context, particularly for women who have received a high chance NIPT result, and staff should ensure that they are familiar with the positive predictive value of the tests they utilise.
- 2.24 Being skilled in delivering information in a non-directive way – that is, making sure each option is equally and fairly presented – is also essential for healthcare professionals who are supporting women to make informed choices about screening. The existing guidance is clear that women should understand that it is their choice whether to have screening or not, and that all staff involved should adopt a non-directive, non-judgmental and supportive approach. However, we heard a number of cases in which women felt that

¹⁸² It is important to note that what is considered to be balanced information is, to some extent, a matter of judgment, and a focus on only positive information might equally be thought to be providing an unbalanced picture of genetic conditions.

¹⁸³ Kratovil AL and Julion WA (2017) Health-care provider communication with expectant parents during a prenatal diagnosis: an integrative review *Journal of Perinatology* 37: 2-12.

they were clearly directed by healthcare staff towards a particular option and not supported in their choices. More subtly, the way in which language is used can convey messages, positive and negative, about a healthcare professional's views on screening choices and about choices to continue or terminate a pregnancy.

"'Risk', 'bad news', 'I'm sorry' and 'abnormality' all provide a nudge towards termination." (Person with a family member or close friend with a genetic condition – survey respondent)

"I spoke to a couple who kept being asked if they would like to terminate their pregnancy and they kept having to say no." (Healthcare professional – survey respondent)

2.25 When NIPT is introduced into the NHS, there must be a sufficient amount of time to discuss the screening tests and the conditions being tested for in order to enable women to make properly considered choices. Some respondents were concerned about there being a lack of time to discuss prenatal screening with a midwife at the one-hour booking appointment. When NIPT is introduced, this will be included in the conversation about screening at the booking appointment, and it is likely that there will be little time to discuss it.

2.26 The provision of accurate and balanced information that supports all screening choices equally well, and the need for sufficient time to discuss any questions and concerns are essential requirements of the introduction of NIPT within the NHS. Some of our respondents were concerned that the lack of risk to the fetus posed by NIPT could lead to NIPT becoming a routine part of pregnancy that women are expected to opt into, undermining the prospects of women being able to give informed consent. Researchers in bioethics have argued that women have a 'right not to know' information about their fetus, and therefore channelling them towards having NIPT would be unethical.¹⁸⁴ In addition, NIPT, it is suggested, may be seen as 'just a blood test' among the many that are carried out on women during pregnancy and that women will not give NIPT the same level of consideration that they would give amniocentesis or CVS. Research suggests that healthcare professionals may view the consent process for prenatal diagnostic testing differently depending upon whether it is an invasive or non-invasive test.¹⁸⁵

"Many patients in my experience go into this sort of test seeking reassurance and in the full expectation that the result will be negative. They are usually not well prepared for the possibility of a positive result, nor are they adequately prepared for what would follow on from this result." (Person with multiple interests in NIPT – survey respondent¹⁸⁶)

2.27 At all stages of the pathway, women should be informed of test results in a way that ensures that the implications of results are understood and that women have timely access to the information and support they require to avoid unnecessary anxiety being caused. This is especially important for NIPT given the possibility of it being seen as diagnostic. The way the results should be delivered will vary depending on what the results reveal and the preferences of the woman or couple. When a prenatal diagnosis is being delivered, research has found that parents commonly require a significant amount of detailed information to process the news, and that parents benefit from written

¹⁸⁴ Brownsword R and Wale J (2016) The development of non-invasive prenatal testing: some legal and ethical questions *Annual Review of Law and Ethics* 24.

¹⁸⁵ van den Heuvel A, Chitty L, Dormandy E *et al.* (2010) Will the introduction of non-invasive prenatal diagnostic testing erode informed choices? An experimental study of health care professionals *Patient Education and Counseling* 78: 24-8.

¹⁸⁶ Survey respondent who is a healthcare professional with a family member or close friend with a genetic condition.

information that they can read when they are ready. Parents were found to feel most confident in their healthcare professional when they were given thorough and concrete explanations of possible causes of the anomaly, options for the fetus during pregnancy and after birth, current success stories and the complete range of functioning they might expect for their child, as well as when this information was communicated to parents quickly, preferably within 24 hours.¹⁸⁷

- 2.28 To ensure NIPT is delivered successfully within the existing fetal anomaly screening pathway, high quality training of the health and social care professionals involved in screening will be of paramount importance. Healthcare professionals must be able: to provide accurate and balanced information about prenatal tests and the conditions being tested for; to provide decision-making support in a non-directive manner; and to deliver results in an appropriate way. This is not a new assertion. Training is currently provided by Public Health England for healthcare professionals who care for women and couples undergoing screening for fetal anomalies.¹⁸⁸ Several charities also provide training on how to deliver good care within the screening and prenatal diagnosis pathways, including Antenatal Results and Choices (ARC) and the Down's Syndrome Association (DSA). The latter runs a training day called 'Tell it Right, Start it Right'. A small evaluation study found that the training was perceived by attendees to significantly increase knowledge of Down's syndrome, confidence in communicating with parents and confidence in delivering a diagnosis.¹⁸⁹ Currently, these training courses are not compulsory and are limited in reach. Some may consider the content to be 'unbalanced' because the training is run by charitable organisations outside of the NHS umbrella. There is a clear need for high quality mandatory training in this area to be delivered within the NHS fetal anomaly screening programme. Combining training on the technical aspects of screening, and the communication and facilitation skills required, along with high quality information on the tested-for conditions, is a significant challenge that will need to be addressed before the introduction of NIPT. We are aware that Public Health England has convened a working group on training and education that has input from parent support charities, and is committed to developing high quality training for healthcare professionals in order to support the introduction of NIPT for Down's, Edwards' and Patau's syndromes in the NHS.

"Meeting people is important because it's meeting them personally and finding out about them...what their journey and their story. Like, you wouldn't think it of many Down syndrome people but we're actually quite sharp and strong people..." (Person with Down's syndrome – interviewee)

Printed and online information

- 2.29 Centrally-produced written resources such as the NHS England booklet *Screening tests for you and baby* and the NHS Scotland booklet *Your guide to screening tests during pregnancy* were considered by many respondents to our survey and consultation to provide a good explanation of the screening tests and a balanced and accurate description of Down's, Edwards' and Patau's syndromes. The NHS Choices website was also thought to provide good, balanced information in both written and video form,

¹⁸⁷ Kratovil AL and Julion WA (2017) Health-care provider communication with expectant parents during a prenatal diagnosis: an integrative review *Journal of Perinatology* **37**: 2-12.

¹⁸⁸ Public Health England (2016) *Antenatal and newborn screening e-learning module*, available at: <https://cpdscreeing.phe.org.uk/annb-elearning>.

¹⁸⁹ Bryant LD, Puri SC, Dix L and Ahmed S (2016) Tell it right, start it right: An evaluation of training for health professionals about Down syndrome *British Journal of Midwifery* **24**: 110-7.

although the website was criticised by some respondents for not including a section on continuation of pregnancy after the diagnosis of a genetic condition. All centrally produced written or multimedia resources will need to be updated to include high quality information about NIPT when it is introduced, and different information resources may need to be developed for different stages of the pathway. Again, we are aware that Public Health England is already committed to producing high quality printed and online information for women and couples, as well as healthcare professionals, to support the introduction of NIPT for Down's, Edwards' and Patau's syndromes in the NHS.

- 2.30 Examples of written information about screening that had been produced by individual NHS hospitals that the Working Group came across included information about Down's syndrome that was out-of-date. Other locally produced information resources tended to focus on the medical problems associated with Down's, Edwards' and Patau's syndromes, with little attention given to the social aspects. The lived experiences of people with Down's syndrome and their families were rarely mentioned, for example, which includes many commonly experienced and positive aspects of the condition. We also came across leaflets produced by NHS hospitals about NIPT for Down's syndrome that was available as a private service within the hospital, which we felt did not clearly communicate the chance of a false positive result with NIPT. The variable quality of locally produced information resources suggests that the development of standardised, high quality information from Public Health England is a matter of priority.

Non-NHS sources of information and support

- 2.31 NHS healthcare professionals and NHS information resources are not the only sources of information and support available to women and couples undergoing screening. Many will search the internet to get information about screening tests and genetic conditions, seek advice from third party organisations and talk to friends and family. This kind of information plays an important role in the extent to which informed choices about screening are being made by women and couples.
- 2.32 There are many organisations that provide information and support to women and couples who would like to know more about Down's syndrome. The Healthtalk.org website, for example, has hundreds of videos of people sharing their health experiences and includes videos about prenatal screening and having a child with Down's syndrome. The NHS Choices website directs users to the Down's Syndrome Association (DSA) website, which provides information about prenatal testing and what life is like for people with Down's syndrome and their families. For women and couples who have decided to continue with a pregnancy following a diagnosis of Down's syndrome, the DSA has produced a booklet called *Looking forward to your baby*.¹⁹⁰ The DSA also runs a helpline that offers information, support and advice. There are numerous other UK and international organisations, websites and informal groups that provide information and personal stories about Down's syndrome, such as Down's Syndrome Scotland, Down Syndrome Research Foundation, Down's Heart Group, Future of Down's, Saving Down Syndrome, and blogs such as Downs Side Up and Force of Nature. There is one support organisation for Edwards' and Patau's syndromes, Support Organisation for Trisomy 13 and Trisomy 18 (SOFT), which provides information about prenatal testing for these conditions and about the conditions themselves.

¹⁹⁰ Down's Syndrome Association (2013) *Looking forward to your baby*, available at: <http://www.downs-syndrome.org.uk/download-package/looking-forward-to-your-baby/>.

- 2.33 ARC is the only national charity in the UK dedicated to supporting parents through decisions around prenatal testing and its potential consequences. ARC describes itself as “offering non-directive information and support to parents before, during and after antenatal screening”¹⁹¹; it is not a counselling service. The NHS Choices website directs pregnant women to ARC’s helpline and website for more information on screening decisions, screening results and options. The ARC website provides information and resources for parents and health professionals on a range of topics including prenatal screening tests, continuing a pregnancy and ending a pregnancy. The organisation’s helpline receives around 5,000 calls and emails each year. In addition, ARC provides training for health professionals on delivering difficult news, supporting parental decisions, and care following a prenatal diagnosis. Several publications are available to pregnant women and couples, including a booklet for those who are considering a termination of pregnancy and a booklet for those who have chosen to continue with their pregnancy.¹⁹²
- 2.34 ARC was originally set up as SATFA (Support After Termination For Abnormality) in 1988, but has evolved to provide support to anyone within the screening pathway, including those yet to make a screening decision. The director of ARC represents the ‘public and patient voice’ as a member of the UK National Screening Committee (UKNSC), and sits on the UKNSC’s Fetal, Maternal and Child Health Reference Group. The role of this reference group is to “advise the UKNSC on issues relating to screening policy in the relevant populations as well as provide a reference group for issues relating to the implementations and improvement of screening programmes.”
- 2.35 Some of the respondents to our consultation were critical of ARC, in that they believed ARC’s origins and current focus present the potential for bias in the support it provides to women. Some respondents considered the language used in its booklet on continuing a pregnancy to be overly negative. One respondent highlighted that, whilst ARC work with women who have miscarried or terminated a pregnancy as ‘peer supporters’, it does not have peer supporters who are parents of a child with a disability. ARC provides training for healthcare professionals on continuing pregnancies following a prenatal diagnosis as part of its training on supporting parental decisions, but it does not specifically involve parents of a disabled child in delivering training. As a charity, ARC needs to secure funding and receives some corporate sponsorship from a number of NIPT manufacturers.
- 2.36 We found no evidence of women being directed towards termination by ARC staff, and its website and materials emphasise the importance of personal choice. ARC staff appear to be highly motivated to provide impartial support and advice and they clearly provide an essential service to many women and their families in difficult situations. As an organisation that is independent of the NHS, ARC has been instrumental in providing evidence to improve services for women within the testing and termination pathway. Through its director, ARC also provides important input at the policy level in terms of representing the women who use their services. However, ARC is the only prenatal testing support organisation to which the NHS directs pregnant women. As such, it is important that it provides balanced, non-directive and impartial advice to parents, and balanced information via training to health professionals. One way to further demonstrate

¹⁹¹ See <http://www.arc-uk.org/>.

¹⁹² Antenatal Results & Choices (2012) *A handbook for parents after a prenatal diagnosis*, available at: <http://www.arc-uk.org/for-parents/publications-2/supporting-you-throughout-your-pregnancy-2>, Antenatal Results & Choices (2012) *A handbook to be given to parents when an anomaly is diagnosed in their unborn baby*, available at: <http://www.arc-uk.org/for-parents/publications-2/supporting-you-throughout-your-pregnancy-2>.

this would be to work more with parents who have chosen to continue a pregnancy following a prenatal diagnosis as peer supporters and to involve them in their professional training, and to continue to forge links with support organisations for people with genetic conditions.

- 2.37 ARC may experience increasing demand for its services following the introduction of NIPT into the NHS. It may require additional resources to continue providing a high quality service. However, some may consider that receiving funding from NIPT manufacturers represents a conflict of interest and challenges ARC's claims of impartiality. Continued sponsorship from NIPT manufacturers could compromise trust in the view of the public and some of its potential service users. This is particularly important when NIPT becomes offered in the NHS as a second stage test following combined screening.

Other factors affecting women's choices

- 2.38 Women's choices about whether to have screening or diagnostic testing and whether to continue with a pregnancy or not following a diagnosis of a fetal anomaly are influenced by a much wider range of factors than simply the information and support they have accessed at the time of screening. These factors include, for example, the views of a partner, general attitudes towards disability, the presentation of disability and prenatal testing in the media, and the perceived impact of a disabled child on the family (see Paragraphs 1.15-1.16). Public Health England might consider providing detailed briefings for journalists when NIPT is introduced to help ensure accurate and balanced information about NIPT and the conditions being tested for is reported in the media. It is important to note, however, that there is no consensus on what is considered to be balanced information, as balance, to a significant extent, is a matter of judgment linked to personal beliefs, values and experience.¹⁹³
- 2.39 Some respondents to the consultation were concerned that the introduction of NIPT may result in women feeling an increased expectation to undergo further testing following a high chance combined test result, given that NIPT is highly accurate and poses no risk to the fetus. This expectation might derive from people around the women and couple, or wider society. The availability of NIPT may lead some women to feel it is harder for them to justify not having further testing and thereby exposes them to stronger pressure to consent to an unwanted investigation.

"Concerns are that you would be considered strange for not wanting to take these tests." (Person with multiple interests in NIPT – survey respondent¹⁹⁴)

"Ease of accessing the tests is likely to lead to societal attitudes that it is a 'duty' to test rather than an option." (Person with a family member or close friend with a genetic condition – survey respondent)

- 2.40 Attitudes towards and perceptions of what it is like to have a child with Down's syndrome or a disability are likely to be formed by a variety of factors such as whether the woman has a personal experience of Down's syndrome or disability and the way in which Down's syndrome and disability is discussed in schools and portrayed in the media.¹⁹⁵ An increasing number of people with Down's syndrome and other disabilities now feature in

¹⁹³ Ahmed S, Bryant L and Hewison J (2007) 'Balance' is in the eye of the beholder: providing information to support informed choices in antenatal screening via antenatal screening web resource *Health Expectations* **10**: 309-20.

¹⁹⁴ Survey respondent with recent experience of being pregnant and a family member or close friend with a genetic condition.

¹⁹⁵ Scope (2014) *Current attitudes towards disabled people* available at: <http://www.scope.org.uk/Scope/media/Images/Publication%20Directory/Current-attitudes-towards-disabled-people.pdf>.

television programmes and issues relating to disability are given increasing attention by the media. For example, a person with Down's syndrome currently plays a character in Coronation Street, the children's BBC channel CBeebies regularly features disabled children, and the recent documentary 'A World Without Down's Syndrome?' was aired at prime time on BBC television, which generated a large amount of media debate. However, some respondents to our survey and consultation believed that societal attitudes towards Down's syndrome and disability are still overly negative, uninformed or out-of-date. A survey of public perceptions of disabled people found that almost 8 out of 10 respondents felt that there is either a lot or a little prejudice towards disabled people.¹⁹⁶ The introduction of NIPT, it is suggested, might further cultivate negative attitudes towards Down's syndrome, which in turn may affect the choices women make.

- 2.41 A related factor that may affect the choices women make is the state support available for disabled people. Perceptions about how disabled people will be included in the education system, supported to get employment and provided with adequate health and social care may all have an influence. Recent austerity measures are widely thought to be having a disproportionately adverse impact on disabled people in the UK. The perception that state support is inadequate may underlie some women's concerns about who will care for their child when they and their partner have died (see Paragraph 2.56).

Prenatal diagnoses

- 2.42 The extent to which the introduction of NIPT as a second stage test in the NHS prenatal screening programme will affect the numbers of women choosing to continue or terminate their pregnancies has been the subject of much speculation and concern. The authors of the RAPID study estimate that offering NIPT as a second stage test across the whole NHS will lead to 195 more fetuses with Down's syndrome identified by NIPT or diagnostic testing per year. Of these, it is estimated that 111 would receive a confirmed diagnosis following diagnostic testing. Rates of termination following a fetal diagnosis of Down's syndrome have ranged from 89 to 95 per cent between 1989 and 2013. It seems likely, therefore, that a high proportion of the additional 111 women whose fetuses have a diagnosis of Down's syndrome will choose to terminate their pregnancies and a small proportion will choose to continue their pregnancies. The RAPID study authors predict a further 84 fetuses will be identified each year as being very likely to have Down's syndrome following NIPT where no further testing is undertaken. Early evidence from the RAPID study suggests it is likely that most women in this situation will continue their pregnancy.¹⁹⁷
- 2.43 It can be concluded from the RAPID study that the introduction of NIPT in the NHS is likely to result in more women being faced with difficult choices about whether to have a termination or to continue their pregnancies. The overall *proportion* of terminations of pregnancy following a diagnosis of Down's syndrome is likely to fall, but the *number* of terminations is likely to increase. In effect, the introduction of NIPT as a second stage test is likely to lead in numerical terms to both more terminations of pregnancy following a diagnosis of Down's syndrome and more pregnancies being continued than is currently the case. The RAPID study does not make any predictions of how the introduction of

¹⁹⁶ Office for Disability Issues (2011) *Public perceptions of disabled people: Evidence from the British Social Attitudes Survey 2009*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/325989/ppdp.pdf.

¹⁹⁷ Chitty LS, Wright D, Hill M *et al.* (2016) Uptake, outcomes, and costs of implementing non-invasive prenatal testing for Down's syndrome into NHS maternity care: prospective cohort study in eight diverse maternity units *British Medical Journal* **354**: i3426.

NIPT will affect prenatal diagnoses of fetuses with Edwards' and Patau's syndromes, as screening for these conditions had not yet been implemented in all of the participating hospitals.

- 2.44 The RAPID study involved relatively small numbers of women and a research protocol that ensured all healthcare professionals delivering the screening received high quality, comprehensive training in supporting informed decision making. In addition, the calculations underpinning the estimates of offering NIPT to pregnant women across the UK were based on a number of assumptions (see Paragraph 2.7). Therefore, it would be unwise to assume that the study is a perfect predictor of uptake, diagnosis and termination rates following the introduction of NIPT across the NHS. In order to consider the different possible scenarios, the following sections discuss the potential implications of an increase in both the number of women continuing a pregnancy and in the number of women terminating a pregnancy.

Continuation of pregnancy

- 2.45 There are a number of potential benefits associated with receiving a prenatal diagnosis of Down's, Edwards' or Patau's syndromes for women and couples who would wish to continue their pregnancy.¹⁹⁸ A prenatal diagnosis can help women and couples to prepare psychologically and practically for the birth of a baby with a genetic condition. It can reduce the potential harms associated with receiving a diagnosis at or soon after birth, as a number of factors can mean that this situation is not optimal for receiving what some women and couples would regard as difficult news. The anxiety and uncertainty generated by a postnatal diagnosis relating to a lack of understanding about the condition and its implications, compounded by the physical aspects of childbirth and potential health threats to the baby, can make the assimilation of new information at this time extremely challenging. A prenatal diagnosis, on the other hand, can mean having time to understand and accept the diagnosis, to seek information and advice from support groups and other parents and to put any practical arrangements in place for after the birth, such as sourcing any special equipment or arranging additional childcare support.

"The benefit for me was that it was an opportunity for me to learn and educate myself before the arrival of my beautiful baby." (Woman with experience of undergoing NIPT – interviewee)

"I think it's a good thing that they know...what they are expecting. They know exactly what to do. How to treat the baby...They might not know, parents might now know what it'll be like." (Person with Down's syndrome – interviewee)

- 2.46 In some cases, the fetus will not be expected to survive the pregnancy or for very long after birth. Knowing in advance that their baby is likely to die may not make it any easier for parents and those around them. However, it can give parents more time to prepare for the death of their child, to consider any mementos and keepsakes they would like to create and to make arrangements for a ceremony or funeral. A prenatal diagnosis can provide parents with an explanation for the death of their baby, which can be helpful for some. It has been suggested that women who continue a pregnancy following a prenatal diagnosis of an anomaly or condition that means the fetus is unlikely to survive pregnancy or the newborn period can have improved psychological outcomes compared to women who choose to terminate their pregnancies. One possible reason for this is

¹⁹⁸ Ralston SJ, Wertz D, Chelmon D, Craigo SD and Bianchi DW (2001) Pregnancy outcomes after prenatal diagnosis of aneuploidy *Obstetrics and Gynecology* **97**: 729-33.

that women who continue a pregnancy receive more support from family and friends as the loss of a newborn is a more visible and socially acceptable loss than termination of a pregnancy.¹⁹⁹

"If life threatening, can give families time to make memories. Give them an answer and make them feel prepared." (Person with a genetic condition – survey respondent)

"Even in all the sadness that we were going through when [our daughter] was born, there was still so much joy, because we'd had time to prepare ourselves." (Woman with experience of undergoing NIPT - interviewee)

- 2.47 A prenatal diagnosis also allows medical interventions to be offered that can potentially improve the outcomes for the baby. There are no NHS standards or guidelines on antenatal care for women continuing a pregnancy after a diagnosis of a fetal anomaly, but RCOG recommends that such women should be cared for either at a fetal medicine unit or in conjunction with her referring obstetrician. RCOG suggests that women should be referred to specialists such as paediatricians, paediatric surgeons or neonatologists to plan for the birth, and that the baby may need to be born in a centre with immediate access to a range of paediatric specialists, such as cardiologists or paediatric surgeons. If the fetus is unlikely to survive long after birth, the provision of palliative care after delivery can be discussed and planned. In either instance, RCOG recommends that a coordinated care pathway needs to be established and women should have easy access to a designated health professional throughout the pregnancy.²⁰⁰
- 2.48 Many of the complications commonly associated with Down's syndrome, such as heart defects and intestinal problems, often can be successfully treated with postnatal surgery or other postnatal treatments, meaning that there is little motivation to develop prenatal interventions for these kinds of complications, particularly given the high risk of harm to the fetus and pregnant woman that such interventions could pose. The medical management of babies born with Edwards' or Patau's syndromes is more controversial in terms of providing active care versus palliative or comfort care. Research suggests that parents need to be involved in making decisions about these options and that, in cases where assumptions are made about the need for palliative care, this is a contributing factor to the high neonatal mortality rates of babies with these syndromes, which in turn impacts on parental decision making.²⁰¹
- 2.49 Researchers are attempting to develop prenatal therapies that focus on brain development in fetuses with Down's syndrome. The potential to affect brain development is greater in fetuses than in children and adults and studies have shown that prenatal drug treatment is effective at improving the cognition of mice with trisomies.²⁰² Other researchers have made initial steps, using advanced genome editing techniques, towards the development of 'chromosome therapy' for Down's syndrome.²⁰³ This kind of

¹⁹⁹ Cope H, Garrett ME, Gregory S and Ashley-Koch A (2015) Pregnancy continuation and organizational religious activity following prenatal diagnosis of a lethal fetal defect are associated with improved psychological outcome *Prenatal diagnosis* **35**: 761-8.

²⁰⁰ Royal College of Obstetricians and Gynaecologists (2010) *Termination of pregnancy for fetal abnormality in England, Wales and Scotland*, available at: <https://www.rcog.org.uk/globalassets/documents/guidelines/terminationpregnancyreport18may2010.pdf>.

²⁰¹ Carey JC (2012) Perspectives on the care and management of infants with trisomy 18 and trisomy 13: striving for balance *Current Opinion in Pediatrics* **24**: 672-8.

²⁰² Guedj F and Bianchi DW (2013) Noninvasive prenatal testing creates an opportunity for antenatal treatment of Down syndrome *Prenatal diagnosis* **33**: 614-8.

²⁰³ Jiang J, Jing Y, Cost GJ et al. (2013) Translating dosage compensation to trisomy 21 *Nature* **500**: 296-300.

research has the potential to be controversial. Some do not view Down's syndrome as a condition or disease to be cured or treated, but consider it to be integral to the essence and personality of the person with Down's syndrome.²⁰⁴ If effective prenatal treatments for Edwards' and Patau's syndromes were to be developed, however, it is likely that these would be widely welcomed given the life-limiting effects of these conditions. Effective prenatal treatments for Down's, Edwards' and Patau's syndromes do not appear to be on the immediate horizon but, if they were to become available in future, they could be reasonably expected to have an impact on the decisions that women and couples make about prenatal screening.

Termination of pregnancy

2.50 There were a range of views among the people we consulted during the project on the possibility of the introduction of NIPT leading to an increase in the number of women having a termination following a prenatal diagnosis of Down's, Edwards' and Patau's syndromes in England, Wales and Scotland (termination on the grounds of fetal anomaly is illegal in Northern Ireland). In this section we examine the issues that were raised in relation to a possible increase in terminations, which primarily related to Down's syndrome.

2.51 The ability of individuals to make free, informed choices is considered to be an important value within healthcare. An increase in the number of terminations may not be considered problematic by those who believe individual choice about termination to be the principal relevant value. However, people with this view might still be concerned about a possible net increase in harm to women from more terminations taking place, relating to the distress and anxiety experienced by women who have a termination after a diagnosis of fetal anomaly.²⁰⁵ An increase in terminations after a fetal diagnosis of Down's syndrome is likely to be problematic for people who believe Down's syndrome is not sufficient grounds for termination and who might, on this basis, disagree with screening for Down's syndrome altogether.²⁰⁶ An increase in terminations is likely to be problematic for people who disagree with termination on any grounds, whose views may be related to concerns about harm to fetuses. As stated previously, a review of UK abortion law is outside the scope of this project and therefore we take the current law as the backdrop of our discussions and conclusions.

"I don't agree with anything that takes life away...because life is precious, life is valuable." (Person with Down's syndrome – interviewee)

"I'm a pro-choice person. I believe what the woman wants she should get. If she doesn't want a baby with Down's syndrome she doesn't have to... It's a woman's rights." (Person with Down's syndrome – interviewee)

2.52 An increase in terminations, or any termination, could be problematic if the information being provided to women about Down's syndrome was overly negative or out-of-date, if

²⁰⁴ New York Times Blog (2010) *Should down syndrome be cured?*, available at:

http://parenting.blogs.nytimes.com/2010/01/11/should-down-syndrome-be-cured/?_r=2.

²⁰⁵ It is important to note, however, that although a small number of women do report regretting their decision to have a termination, most do not (see Paragraph 1.17).

²⁰⁶ It should be noted that some people are opposed to termination at any gestational stage on the grounds of fetal anomaly. For example, a Private Members Bill set before Parliament by Lord Shinkwin – the Abortion (Disability) Bill (HL) 2016-117 – proposes that the ground for legal abortion at any gestational stage that "there is a substantial risk that if the child were born it would suffer from such physical or mental abnormalities as to be seriously handicapped" should be removed from the Abortion Act 1967. At the time of writing, the Bill received support at the Second Reading and Committee stage, and will next go through to the Report stage in February 2017. See: <http://services.parliament.uk/bills/2016-17/abortiondisabilityequality.html>.

screening and termination became routine, if a diagnostic test had not been carried out to confirm the diagnosis, or if women were experiencing pressure or perceived expectation to terminate their pregnancy. On this latter point, it should be acknowledged that women and couples are likely to feel a time pressure when making decisions about termination. This makes it all the more important to ensure that women understand before they embark on screening that it might mean they will be faced with a decision about termination if a genetic variation is found. Overall, the need for accurate, balanced and non-directive information and sufficient time to discuss any questions and concerns with skilled health and social care professionals is especially important in the light of a potential increase in prenatal diagnoses of Down's syndrome.

Concerns about a reduction in the incidence or prevalence of people with Down's syndrome

- 2.53 Some concerns about an increase in terminations relate to a possible reduction in the number of people with Down's syndrome and the harm that this could cause them. The rate of terminations is one of a number of factors that can influence the incidence (the number of babies born in a year) and prevalence (the proportion of people with the condition) of people with Down's syndrome (see Paragraph 1.13). It is therefore uncertain whether or to what degree the introduction of NIPT will lead to a reduction in the incidence or prevalence of Down's syndrome, even if it does result in an increase in the number of terminations. However, this is a possibility and it is worth exploring the potential implications.
- 2.54 Some respondents to our survey and consultation were concerned that a reduction in the incidence or prevalence of people with Down's syndrome would mean that existing or future individuals would be harmed. For example, there was concern that there would be less specialised state support and care, a loss of skills and experience among those caring for or educating people with a learning disability, less money directed towards research to improve the lives of people with Down's syndrome and an increase in discrimination, exclusion and abuse. Such outcomes, in addition to being undesirable in themselves, could have an impact on the choices women make following a diagnosis in the future. There is a lack of research and evidence that establishes any robust causal link between the incidence or prevalence of a given condition and these possible negative effects. However, it is possible to examine the plausibility of these effects occurring.
- 2.55 State support and care can be broken down into healthcare, specialist support at nursery, primary and secondary school and further education, social support, support in entering employment and support in old age. In the UK, there have been widespread changes in how society supports and integrates disabled people. In September 2014, the Children and Families Act came into effect, which brought in reforms to ensure services and support are delivered for disabled children and young people and those with special educational needs.²⁰⁷ This legal change and broader societal shifts are not likely to be dependent on the incidence or prevalence of one particular condition. Similarly, estimates suggest that learning disabilities affect approximately one million people in the UK (one to two per cent of the population),²⁰⁸ although this number may be higher

²⁰⁷ Part 3 of Children and Families Act 2004, available at: <http://www.legislation.gov.uk/ukpga/2014/6/contents/enacted>.

²⁰⁸ Public Health England (2014) *People with learning disabilities in England 2013*, available at: https://www.improvinghealthandlives.org.uk/securefiles/170215_1849/People%20with%20learning%20disabilities%20in%20England%202013.pdf.

depending on how learning disability is defined, and the large majority cannot be attributed to a genetic cause such as Down's syndrome. Therefore, services to support people with learning disabilities will be required irrespective of the incidence or prevalence of people with Down's syndrome. In 2011, it was predicted that there would be sustained growth in the need for social care services for adults with learning disabilities over the next 15 years.²⁰⁹

- 2.56 This is not to dismiss concerns about the current levels of state support available for people with physical and intellectual disabilities. The UN Committee on the Rights of Persons with Disabilities reported in June 2016 serious concerns about the disproportionate adverse impact of austerity measures on the rights of disabled people in the UK.²¹⁰ A recent House of Lords Select Committee report on the Equality Act concluded that the Government is failing in its duty of care to disabled people.²¹¹ Further, an independent inquiry carried out between 2010 and 2013 into the deaths of 247 people with learning disabilities found that 42 per cent of the deaths were premature. The most common reasons for these deaths were delays or problems with diagnosis or treatment and problems with identifying needs and providing appropriate care in response to changing needs.²¹² A recent review of the care and support provided to children with learning disabilities, autism and mental health in the UK highlighted instances of serious poor practice and made recommendations for improvements that could be made to the current system.²¹³
- 2.57 It is difficult to say whether the quality of health and social care received by people with Down's syndrome would be affected if the incidence or prevalence of the condition were to be reduced. There is some evidence that people with less common conditions encounter problems in accessing high quality care. For example, a survey of patients and families living with a rare disease found that patients often have difficulties securing the correct diagnosis and that patients and families struggle to access information on their condition and experience a lack of support with both their medical and non-medical needs. Patients also reported badly coordinated care, particularly around the time of transition from paediatric to adult services, and difficulty accessing all of the services they require.²¹⁴ Currently, the care of children with Down's syndrome is usually managed by a community paediatrician, who will coordinate input from allied health professions such as audiology, physiotherapy, speech and language therapy and occupational therapy. Health surveillance is taken over by GPs once they reach adulthood. There are few specialists in Down's syndrome in the UK and no specific centre for medical care for people with Down's syndrome. However, the Down Syndrome Medical Interest Group is a network of doctors who aim to promote interest in the management of the syndrome and who work to produce guidelines on best medical practice. There are no specific NICE

²⁰⁹ Improving Health and Lives Learning Disabilities Observatory (2011) *Estimating future need for social care among adults with learning disabilities in England: an update*, available at: https://www.improvinghealthandlives.org.uk/securefiles/170215_1850//HLaL2011-05FutureNeed.pdf.

²¹⁰ United Nations Committee on the Rights of Persons with Disabilities (2016) *Inquiry concerning the United Kingdom of Great Britain and Northern Ireland carried out by the Committee under article 6 of the Optional Protocol to the Convention on the Rights of Persons with Disabilities*, available at: http://tbinternet.ohchr.org/_layouts/treatybodyexternal/TBSearch.aspx?Lang=en&TreatyID=4&DocTypeCategoryID=7.

²¹¹ House of Lords Select Committee on the Equality Act 2010 and Disability (2016) *The Equality Act 2010: the impact on disabled people*, available at: <http://www.publications.parliament.uk/pa/ld201516/ldselect/ldeqact/117/117.pdf>.

²¹² Heslop P, Blair PS, Fleming P *et al.* (2014) The Confidential inquiry into premature deaths of people with intellectual disabilities in the UK: a population-based study *The Lancet* **383**: 889-95, Heslop P, Blair P, Fleming P *et al.* (2013) *Confidential Inquiry into premature deaths of people with learning disabilities (CIPOLD): final report*.

²¹³ Council for Disabled Children (2017) *These are our children. A review by Dame Christine Lenehan commissioned by the Department of Health*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/585376/Lenehan_Review_Report.pdf.

²¹⁴ Rare Disease UK (2010) *Experiences of rare diseases: an insight from patients and families*, available at: <http://www.raredisease.org.uk/media/2362/rduk-family-report.pdf>.

guidelines pertaining to Down's syndrome, but there are disease-specific growth charts as well as developmental schedules that are particular to children with Down's syndrome.

- 2.58 There have been improvements in medical care and health outcomes for people with Down's syndrome in recent years. These improvements have not been a result of advances in understanding of Down's syndrome itself, but in managing its related conditions. For example, the management of heart defects associated with Down's syndrome has been revolutionised in the last 50 years due to advances in virtually all aspects of paediatric cardiovascular medicine and surgery.²¹⁵ Fifty per cent of children with Down's syndrome have congenital heart disease, but in less than 20 per cent of children with congenital heart disease can it be attributed to a known cause such as a chromosomal anomaly.²¹⁶ This would indicate that medical advances in paediatric cardiology would have progressed irrespective of the incidence and prevalence of Down's syndrome. The same is likely to be true for advances in paediatric surgery, ear, nose and throat services, endocrinology and the other specialties that attend to the health problems associated with Down's syndrome.
- 2.59 In the case of research funding, market forces in the private sector and aims to make efficient use of state resources in the public sector would indicate that common health conditions affecting greater numbers of people are likely to take priority in research and in the development of treatments. The prevalence of a given condition features in the criteria used by research funders such as the Wellcome Trust, the Medical Research Council (MRC) and the National Institute for Health Research (NIHR). The MRC, for example, dedicates 10 per cent of its available grant resources to research into rare disease, which it defines as diseases affecting fewer than 1 in 10,000 people. In Australia there is a significant relationship between research funding and burden of disease measures, although analyses of National Institute for Health (NIH) funding in the USA have shown that disease-specific research funding does not necessarily correlate with disease burden.²¹⁷ There is an EU Regulation on orphan medicinal products that aims to promote investment in research on medicines to treat patients with rare diseases, which are defined as conditions that affect no more than five in 10,000 people.²¹⁸ However, there would need to be a significant change in the prevalence of people with Down's syndrome for it to be considered rare under the MRC's or the EU's definitions. But again, this is not to dismiss concerns about current levels of funding of research into Down's syndrome. There is the suggestion that federal funding for Down syndrome research in the USA has decreased in recent years.²¹⁹
- 2.60 Several respondents to the survey and consultation raised concerns about people with Down's syndrome and their families experiencing more discrimination, social exclusion or abuse if the incidence or prevalence of people with Down's syndrome decreased

²¹⁵ Freedom RM, Lock J and Bricker JT (2000) Pediatric cardiology and cardiovascular surgery: 1950–2000 *Circulation* **102**: Iv-58-Iv-68.

²¹⁶ Blue GM, Kirk EP, Sholler GF, Harvey RP and Winlaw DS (2012) Congenital heart disease: current knowledge about causes and inheritance *Medical Journal of Australia* **197**: 155-9.

²¹⁷ Aoun S, Pennebaker D and Pascal R (2004) To what extent is health and medical research funding associated with the burden of disease in Australia? *Australian and New Zealand journal of public health* **28**: 80-6; Gillum LA, Gouveia C, Dorsey ER et al. (2011) NIH disease funding levels and burden of disease *PLoS one* **6**: e16837.

²¹⁸ Regulation (EC) No 141/2000 of the European Parliament and of the Council on Orphan Medicinal Products, available at: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:018:0001:0005:en:PDF>.

²¹⁹ Disability Scoop (2012) *Funding for Down syndrome research shrinks*, available at: <https://www.disabilityscoop.com/2012/02/24/funding-down-syndrome-shrinks/15058/>.

following the introduction of NIPT. This would be contrary to the aspirations of most societies to cultivate an equal and inclusive environment for all of its citizens.

“...Not all women will want testing but it's likely that the number of these children born will reduce - this may make them more liable to discrimination or prejudice as people become less likely to see them.” (Healthcare professional – survey respondent)

“I think, for me, I'd like to have more Down syndrome people...” (Person with Down's syndrome – interviewee)

“Those remaining could experience additional discrimination as could their families as society becomes less willing to support those who are seen as a burden on resources.” (Person with a family member or close friend with a genetic condition – survey respondent)

- 2.61 It would be difficult to establish a causal link between a reduced incidence or prevalence of a condition and increased discrimination, given the other factors that are likely to be involved, and we are unaware of any evidence supporting this claim. Many disabled people, regardless of how common or rare their condition is, experience discrimination, exclusion, violence and abuse, with people with learning disabilities at the highest risk.²²⁰ The Equality and Human Rights Commission and the Equality Commission for Northern Ireland have ongoing programmes of work to address disability related harassment and promote disabled people's safety and security.²²¹
- 2.62 In summary, it is uncertain whether the introduction of NIPT will lead to a significant reduction in the incidence or prevalence of people with Down's, Edwards' and Patau's syndrome. If a reduction does occur, it is difficult to predict what will be the consequences of this for people with the syndromes, harmful or otherwise. However, in considering the consequences of a significant reduction in Down's syndrome, it is plausible that the quality of specialist health and social care received by people with Down's syndrome, and the importance attributed to research into Down's syndrome will be affected.

The timing of termination

- 2.63 It is possible that the introduction of NIPT in the NHS prenatal screening programme may affect the timing of terminations, as well as the number of terminations. Again, it is uncertain what the effect will be, but as already discussed, one possible outcome of offering NIPT as a second stage test is a delay in diagnosis for some women. For women who want a termination, this could lead to a termination taking place a week or more later than if they had had a diagnostic test directly after the combined test (see Paragraph 2.15).
- 2.64 A further possible effect of the introduction of NIPT in the NHS is a reduction in the number of late terminations taking place. Two-hundred and thirty terminations (0.1 per

²²⁰ For example, see: BBC News (2015) *Sexual abuse of disabled adults revealed*, available at: <http://www.bbc.co.uk/news/uk-32693998>, Equality and Human Rights Commission (2009) *Promoting the safety and security of disabled people*, available at: <http://arcuk.org.uk/safetynet/files/2012/08/Promoting-safety-and-security-of-disabled-people.pdf>; Petersilia J (2001) Crime victims with developmental disabilities: a review essay *Criminal Justice and Behavior* 28: 655-94.

²²¹ Equality and Human Rights Commission (2013) *Manifesto for change: progress report 2013*, available at: https://www.equalityhumanrights.com/sites/default/files/manifesto_for_change_progress_report_2013_final.pdf; Equality Commission for Northern Ireland (2012) *Strengthening protection for disabled people. Proposals for reform - full report*, available at: <http://www.equalityni.org/ECNI/media/ECNI/Publications/Delivering%20Equality/Disabilitylawreformproposalsfullreport2012.pdf>.

cent of the total) were performed after 24 weeks in England and Wales in 2015.²²² A common reason for a late termination is the ultrasound scan at 18-20 weeks revealing fetal anomalies that were not picked up by earlier screening tests.²²³ Following this, it can take three to five working days for the woman to see a specialist, when she may choose to have further scans and tests. It can take 3-14 days (depending on the analysis method used) to receive results from diagnostic testing, and then the woman and couple may need time to make a decision about continuing or terminating the pregnancy.²²⁴ If, as predicted, Down's syndrome is detected in more fetuses when NIPT is introduced as a second stage screening test following the combined test, this might result in some late terminations being avoided. Some research suggests that earlier terminations are associated with lower levels of stress for women than later terminations, at least in the short term.²²⁵ In addition, those who take a proportional or gradualist view of the fetus are likely to view earlier terminations as less harmful, and less wrong, than later terminations (see Paragraph 1.49).

Other implications for people with genetic conditions

The 'expressivist objection'

2.65 In addition to the potential implications of a possible reduction in the prevalence or incidence of people with Down's syndrome (see Paragraphs 2.53-2.62), it has been argued that the introduction of NIPT could have other harmful effects on people with Down's syndrome through the hurtful or disparaging message it sends. This is often called the 'expressivist objection' to prenatal screening, which is sometimes made by those who argue that prenatal screening for disability and the termination of the fetuses that might result communicates to disabled people something about how they are valued by society, and may constitute in itself a form of discrimination or harm.²²⁶ The introduction of NIPT in the NHS, which is likely to result in an increased number of prenatal diagnoses of Down's, Edwards' and Patau's syndromes, could be seen to reinforce or amplify the negative messages sent by existing prenatal screening programmes.

"...It makes me feel like I'm not wanted in society. And no one loves us..." (Person with Down's syndrome – interviewee)

"The screening programme might be interpreted by these people as sending the message that society would have preferred it had they not been born." (Dr Felicity Boardman, Warwick Medical School – consultation respondent)

2.66 There has been considerable criticism of the expressivist objection in the academic literature. Some suggest that any negative messages about disabilities or conditions that

²²² Department of Health (2016) *Abortion statistics, England and Wales: 2015*, available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/570040/Updated_Abortion_Statistics_2015.pdf

²²³ According to some studies, approximately 16 per cent of women will receive a false negative result from the combined test:

Taylor-Phillips S, Freeman K, Geppert J et al. (2015) *Systematic review and cost-consequence assessment of cell-free DNA testing for T21, T18 and T13 in the UK – final report*, available at:

https://legacyscreening.phe.org.uk/policydb_download.php?doc=552.

²²⁴ Public Health England (2015) *Fetal anomaly screening programme standards 2015-16*, available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/421650/FASP_Standards_April_2015_final_2_.pdf.

²²⁵ Daugirdaite V, van den Akker O and Purewal S (2015) Posttraumatic stress and posttraumatic stress disorder after termination of pregnancy and reproductive loss: a systematic review *Journal of Pregnancy* **2015**: 646345.

²²⁶ Parens E and Asch A (2000) *Prenatal testing and disability rights* (Washington, DC: Georgetown University Press).

are communicated by a decision to undergo genetic screening do not extend to the people who have the disability or condition. In other words, it is possible to disvalue a medical condition but still value people who have the condition.²²⁷ Others argue that if the hurtful message sent by prenatal screening was sufficient justification for not screening, it might also suggest that we should not attempt to treat or cure disability, or that it would not be wrong to deliberately bring about disability.²²⁸ It has also been suggested that the wide range of beliefs, doubts and motivations underlying women's decisions to undergo prenatal screening and terminate a pregnancy are so diverse that there is not any single message communicated by individual acts of screening.²²⁹

- 2.67 Some academics are more persuaded by the notion that national health policies permitting prenatal screening and selective termination, rather than individual decisions, can convey harmful messages about the societal value placed on disabled people. When a state sanctions such policies, according to this view, it implicitly endorses selective termination for disability, with implications for the societal standing of disabled people. Defenders of a liberalist approach respond that governments simply make prenatal testing available and remain neutral on whether or not people should use it. However, in reality, this may not reflect the influence that a state decision to allow prenatal testing, or make it available in publicly funded health care services, can have on members of its society.²³⁰ This kind of influence might have implications for wider societal attitudes to disabled people in terms of acceptance, inclusion and tolerance.²³¹ In addition, disapproval of the decisions that families make may encourage the 'privatisation' of disability, from which perspective it may be seen as the family's responsibility to meet the needs of disabled people and no longer as the responsibility of the state. Several respondents to the survey and consultation were concerned about the harmful effect of the introduction of NIPT on the discrimination experienced by people with genetic variations and their families.

"We believe NIPT will not only perpetuate discrimination against people born and unborn with DS [Down's syndrome], but also their parents." (Down Syndrome Research Foundation UK – consultation respondent)

"There are fears that the increasing availability and use of NIPT might result in greater stigmatisation and discrimination against individuals and families with genetic conditions." (PHG Foundation – consultation respondent)

- 2.68 Whether or not it is warranted to see prenatal screening as conveying any message about the value of particular groups of people, the availability of prenatal testing and screening programmes may, as a matter of fact, upset, distress or offend some disabled people.

²²⁷ Malek J (2010) Deciding against disability: does the use of reproductive genetic technologies express disvalue for people with disabilities? *Journal of Medical Ethics* **36**: 217-21.

²²⁸ Buchanan A, Brock D, Daniels N and Wikler D (2000) *From chance to choice: genetics and justice* (Cambridge: Cambridge University Press); McMahan J (2006) Is prenatal genetic screening unjustly discriminatory? *Virtual Mentor* **8**: 50-2.

²²⁹ Nelson JL (2000) Prenatal diagnosis, personal identity, and disability *Kennedy Institute of Ethics Journal* **10**: 213-28; Buchanan A (1996) Choosing who will be disabled: Genetic Intervention and the Morality of Inclusion *Social Philosophy and Policy* **13**: 18-46.

²³⁰ Shakespeare T (1998) Choices and rights: eugenics, genetics and disability equality *Disability & Society* **13**: 665-81.

²³¹ Nelson JL (2000) Prenatal diagnosis, personal identity, and disability *Kennedy Institute of Ethics Journal* **10**: 213-28; Higuchi EC, Sheldon JP, Zikmund-Fisher BJ and Yashar BM (2016) Non-invasive prenatal screening for trisomy 21: consumers' perspectives *American Journal of Medical Genetics Part A* **170a**: 375-85.

"We will be phased out. I find it so offensive." (Person with a genetic condition – survey respondent)

- 2.69 If prenatal screening programmes are to continue, then consideration should be given to how any harmful messages or effects on disabled people might be mitigated. It has been suggested that any expressive effect of screening programmes might be offset by better acknowledging the lived experience of disability and challenging the generalisation that caring for a disabled child is always more burdensome than caring for a non-disabled child. This acknowledgement might be made in a number of arenas, including within health and social care services, in the media, and in government policy making.²³²

Concerns about eugenics

- 2.70 Concerns about the incidence or prevalence of Down's syndrome and about Down's syndrome disappearing altogether following the introduction of NIPT in the NHS, were sometimes expressed by respondents to our survey and consultation alongside warnings about eugenics.

"CARE is of the view that NIPT would negatively impact babies with trisomies, such as Down's syndrome – effectively having an inadvertent eugenic effect – essentially screening them out." (Christian Action Research and Education (CARE) – consultation respondent)

- 2.71 Worries about eugenics are commonly raised within discussions of genetic technologies and genetic research and there is a wide literature on the nature, purpose and ethics of eugenics.²³³ These issues were explored in the Council's 2002 report *Genetics and human behaviour: the ethical context*, which addressed questions relating to the nature and potential uses of research into human behaviour and the genetic bases of traits such as intelligence.²³⁴ As is observed in that report, the controversial history of eugenics and its association with compulsory sterilisation programmes, forced euthanasia, racism and genocide in 1930s Germany is likely to form part of the reason that many object so vehemently to any intervention that might be viewed as eugenic.
- 2.72 But considered more broadly, eugenics need not involve force and may involve any attempt to improve the genetic traits of a population by influencing genetic characteristics.²³⁵ The exact meaning of the term 'eugenics' and what it involves is not widely agreed upon, and distinctions between positive and negative,²³⁶ weak and

²³² McMahan J (2005) Preventing the existence of people with disabilities, in *Quality of life and human difference: genetic testing, health care and disability*, Wasserman D, Bickenbach J, and Wachbroit R (Editors) (Cambridge: Cambridge University Press).

²³³ For a discussion, see: Goering S (2014) Eugenics, in *The Stanford encyclopedia of philosophy*, Zalta E (Editor), available at: <http://plato.stanford.edu/archives/fall2014/entries/eugenics>.

²³⁴ Nuffield Council on Bioethics (2002) *Genetics and human behaviour: the ethical context*, available at: <http://nuffieldbioethics.org/wp-content/uploads/2014/07/Genetics-and-human-behaviour.pdf>.

²³⁵ It has been said that the 'common core' of most definitions of eugenics is that: "...Eugenics is the attempt to improve the human gene pool. People can agree on that definition, even if they disagree considerably about what counts as eugenics". (Wilkinson S and Garrard E (2013) *Eugenics and the ethics of selective termination*, available at: <https://www.keele.ac.uk/media/keeleuniversity/ri/risocsci/eugenics2013/Eugenics%20and%20the%20ethics%20of%20selective%20reproduction%20Low%20Res.pdf>) and in *Genetics and Human Behaviour: the ethical context* the Council said: "The literal meaning of the term eugenics is 'well born'. It refers to the doctrine that humanity can be improved by selective breeding, that is, by encouraging those with desirable traits to reproduce or discouraging those with undesirable traits from doing so" (ibid).

²³⁶ 'Positive eugenics' involves encouraging or actively forcing healthy people with 'good genes' to procreate with one another, whilst 'negative eugenics' involves discouraging or preventing those with less good health and less good genes, from

strong²³⁷ and authoritarian and liberal²³⁸ eugenics have been made. Much of what people typically oppose as eugenic concerns the notion of state-led, coerced, strong or authoritarian eugenic programmes, associated with sometimes ideologically-motivated efforts to minimise the incidence of certain traits in a population. Understood in this way, certain interventions with eugenic outcomes that do not involve force or prejudice might be considered acceptable, in some circumstances.

- 2.73 The notion of 'liberal eugenics', in which women and couples make individual choices about whether to make use of reproductive technologies to influence the genetics of their children, has, for instance, been discussed and defended in recent times by a number of contemporary bioethicists.²³⁹ Defenders of liberal eugenics typically invite a comparison between eugenic interventions and treatment of disease. Most believe that there is value in treating and preventing ill health in existing people since we take disease to cause suffering, limit functioning or interfere with individuals' life projects and ambitions. Efforts to minimise these harms through the use of genetic technologies may be acceptable for similar reasons. However, advocates of liberal eugenics tend to argue that reproductive interventions that are capable of improving the genetics of future children are acceptable only when they are freely chosen by individual prospective parents, rather than when they are encouraged or imposed by the state.
- 2.74 Others have questioned the assumption that it can never be defensible to pursue public health goals with interventions such as prenatal screening.²⁴⁰ It has been argued that models in which a public health goal to reduce disease is one element of prenatal screening programmes which also support individual choice might be ethically preferable in some respects to those that are based on individual choice alone.²⁴¹ State involvement in the use of genetic technologies might better allow for the control and regulation of their use, and public health models might also avoid problems related to embedding, colluding with or reinforcing problematic social norms, or inadvertently giving rise to other harmful outcomes, which could arise if the use of genetic technologies was left entirely to the choices of individuals. It could be argued for this reason that state supported public health goals to minimise genetic conditions or impairments through screening programmes should not be seen as unacceptable in all cases. Some argue further that there might be duties to make use of some genetic technologies to alter the genetics of future people, either at the level of the individual or the state, as a means of reducing 'natural inequalities'.²⁴²

reproducing at all. See Goering S (2014) Eugenics, in *The Stanford Encyclopedia of Philosophy*, Zalta E (Editor), available at: [://plato.stanford.edu/archives/fall2014/entries/eugenics/](http://plato.stanford.edu/archives/fall2014/entries/eugenics/).

²³⁷ "Strong eugenics could be defined as population-level improvement by control of reproduction via state intervention, such as happened in the 1930s. It is motivated by the social judgement that disabled people's lives are unworthy of life, and/or that society should not have to bear the financial costs of supporting its non-productive members. Weak eugenics could be defined as promoting technologies of reproductive selection via non-coercive individual choices." Shakespeare T (1998) Choices and rights: eugenics, genetics and disability equality *Disability & Society* **13**: 665-81).

²³⁸ Nicholas Agar, for example, defends the use of liberal eugenics as an option for prospective parents to alter the genetics of their children, rather than as a device for use by states to improve the population's gene pool.

²³⁹ See, for instance, Agar N (2008) *Liberal eugenics: In defence of human enhancement* (London: Blackwell Publishing).

²⁴⁰ Wikler (1999) What can we learn from eugenics? *Journal of Medical Ethics* **25**: 183-195.

²⁴¹ Wilkinson S (2015) Prenatal screening, reproductive choice, and public health *Bioethics* **29**: 26-35.

²⁴² Buchanan, Brock, Daniels and Wikler argue that the 'distribution of natural assets' should be thought of as a matter of social justice and, as such, to some extent a state matter (Buchanan A, Brock D, Daniels N and Wikler D (2000) *From chance to choice: genetics and justice* (Cambridge: Cambridge University Press)) Savulescu, Harris and some other defenders of liberal eugenics argue that prospective parents have duties to produce the best children they can. (Savulescu J (2001) Procreative beneficence: why we should select the best children *Bioethics* **15**: 413-26; Harris J (2010) *Enhancing evolution: the ethical case for making better people* (USA: Princeton University Press)) These ideas have been criticised by Parens, Parker and others. (Parens E (1998) Is better always good?: The enhancement project *Hastings Center Report* **28**: s1-s17; Parker M (2007) The best possible child *Journal of Medical Ethics* **33**: 279-83).

2.75 Even when eugenics does not involve coercion or force, there may be other reasons why eugenic practices are problematic or unacceptable. Issues related to the expressivist objection, for example, may apply, since some disabled people may perceive either choices made by individual women and couples to terminate pregnancies following diagnosis of a fetal anomaly, or state-supported programmes to improve the genetic health of the population, as equivalent to efforts to prevent people like them existing, and thereby as hurtful, offensive or discriminatory (see discussion at Paragraphs 2.65-2.69). Alternatively, given the background set of societal norms, prejudices and biases that influence how parents actually make decisions, it could be that any collection of individual choices might closely resemble the outcomes of coerced eugenic programmes based on discriminatory views or prejudice – in other words, eugenics might be an ‘emergent property’ of the whole system.²⁴³ A further issue in the case of Down’s syndrome is that even if it is thought that some eugenic practices might be acceptable to minimise disease and suffering, the lived experience of the condition leads some to dispute that Down’s syndrome is a disease which involves suffering (see Paragraph 1.6). Either way, many of those who defend the use of prenatal screening and other reproductive interventions also concede that concerted and sustained efforts should be made to show that society values disabled people and to ensure that they are provided with the same opportunities as those without disabilities.²⁴⁴

Potential benefits for people with genetic conditions

2.76 In reviewing the impacts of prenatal screening, it is important to consider the potential benefits, as well as the harms, for people with genetic variations in terms of enabling them to make informed choices in pregnancy. These benefits may be particularly relevant to people with or who are carriers of an inherited genetic condition (see Paragraph 3.28), but it could apply to people with Down’s syndrome as well if they have children. People with Down’s syndrome have a 35-50 per cent chance of having a child with the condition where one parent has Down’s syndrome; this chance is even higher where both parents have Down’s syndrome.²⁴⁵ People with genetic conditions can be supportive of prenatal screening programmes. For example, some people with Down’s syndrome have expressed the view that testing for Down’s syndrome can be positive in that it can give parents the time to prepare.²⁴⁶ Screening for Edwards’ and Patau’s syndromes in the first trimester was introduced in April 2016 in England, and the opportunity for people to receive an early diagnosis has been generally welcomed by families of people with these conditions.²⁴⁷

“NIPT can help families prepare for any additional needs their baby may have.”
(Person with a genetic condition – survey respondent)

²⁴³ Duster T (2003) *Backdoor to eugenics* (New York: Routledge); Shakespeare T (1998) Choices and rights: eugenics, genetics and disability equality *Disability & Society* **13**: 665-81.

²⁴⁴ Jonathan Glover, sometimes described as a liberal eugenicist, has said: “...we need to send a clear signal that we do not have the ugly attitudes about disability. It is important to show that what we care about is our children’s flourishing: that this, and not shrinking from creating kinds of people, or some horrible project of cleansing the world of them, is what motivates us.” (Glover J (2006) *Choosing children: genes, disability, and design* (Oxford: Oxford University Press). See also: McMahan J (2005) Preventing the existence of people with disabilities, in *Quality of life and human difference: genetic testing, health care and disability*, Wasserman D, Bickenbach J, and Wachbroit R (Editors) (Cambridge: Cambridge University Press).

²⁴⁵ See: Down’s Syndrome Association (2017) *For new parents: general*, available at: <http://www.downs-syndrome.org.uk/for-new-parents/faqs/general/>.

²⁴⁶ Barter B, Hastings RP, Williams R and Huws JC (2016) Perceptions and discourses relating to genetic testing: interviews with people with Down Syndrome *Journal of Applied Research in Intellectual Disabilities* **May**: 10.1111/jar.12256..

²⁴⁷ Personal communication with SOFT, the support organisation for trisomy 13/18.

Implications for the NHS and practitioners

- 2.77 A number of potential implications for the NHS of the introduction of NIPT were raised by respondents to our survey and consultation that have not been mentioned so far.
- 2.78 First, there was concern about a potential increase in pressure on NHS services if more women opt for follow-on testing after receiving a high chance result from the combined test. Such women should receive counselling with clinicians with expertise in prenatal screening, such as genetic counsellors. It has been recognised that the capacity of genetic counselling services must grow as more people access genetic testing services more generally.²⁴⁸ The Association of Genetic Counsellors and Nurses is currently developing a national workforce planning scheme for genetic counselling services across the UK.²⁴⁹
- 2.79 In addition, women who choose to continue their pregnancy may require specialist care throughout pregnancy. As previously discussed, there are no national standards or guidelines on antenatal care for women with a diagnosis of a fetal anomaly, which some may regard as unusual in the context of NHS care. RCOG recommends that a coordinated care pathway needs to be established that could involve obstetricians, fetal medicine specialists, paediatricians, paediatric surgeons and/or neonatologists.²⁵⁰ There are calls to closely monitor women who have received a high chance NIPT result even when the subsequent diagnosis is negative, due to the potential increase in demands on specialist NHS antenatal services.²⁵¹
- 2.80 Women who chose to have a termination after a diagnosis of fetal anomaly will need access to NHS termination services. There are two main methods of termination. A medical termination involves taking medication to end the pregnancy and can be carried out at any stage of pregnancy. Surgical termination can also be carried out at any stage of pregnancy, although different surgical methods are required at different gestations: vacuum aspiration can be used up to 15 weeks' gestation; dilatation and evacuation (D&E) can be used after 15 weeks. In 2015, 55 per cent of abortions were medical abortions, 40 per cent used the vacuum aspiration method and five per cent used D&E.²⁵² RCOG recommends that women should be offered a choice of method of termination for fetal anomaly, and research suggests that it can be psychologically beneficial for women to have the procedure that best fits their individual emotional coping style.²⁵³ However, we heard anecdotally that surgical terminations are not offered to women past 13 weeks gestation in some areas of the country. A survey of women who had had a termination for fetal anomaly, where the mean gestational age of termination was 17 weeks, found that many of the women were not offered a choice of termination method by the NHS. Most of the women were offered only a medical termination, whereas most women who were offered a choice opted for a surgical method.²⁵⁴ A further study found that medical

²⁴⁸ APPG on Rare, Genetic and Undiagnosed Conditions (2016) *Undiagnosed: genetic conditions and the impact of genome sequencing*, available at: <http://www.raredisease.org.uk/media/1860/final-swan-graduate-report.pdf>.

²⁴⁹ Personal communication with the Association of Genetic Counsellors and Nurses.

²⁵⁰ Royal College of Obstetricians and Gynaecologists (2010) *Termination of pregnancy for fetal abnormality in England, Wales and Scotland*, available at: <https://www.rcog.org.uk/globalassets/documents/guidelines/terminationpregnancyreport18may2010.pdf>.

²⁵¹ Cuckle H, Benn P and Pergament E (2015) Cell-free DNA screening for fetal aneuploidy as a clinical service *Clinical Biochemistry* **48**: 932-41.

²⁵² Department of Health (2016) *Abortion statistics, England and Wales: 2015*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/570040/Updated_Abortion_Statistics_2015.pdf

²⁵³ Kerns J, Vanjani R, Freedman L *et al.* (2012) Women's decision making regarding choice of second trimester termination method for pregnancy complications *International Journal of Gynaecology and Obstetrics* **116**: 244-8.

²⁵⁴ Fisher J, Lohr PA, Lafarge C and Robson SC (2015) Termination for fetal anomaly: are women in England given a choice of method? *Journal of Obstetrics and Gynaecology* **35**: 168-72.

termination was associated with more negative experiences of care and lower acceptability among women, and that acceptability declined with increasing gestational age.²⁵⁵ Whether or not the introduction of NIPT results in more terminations for fetal anomaly, it is important that the delivery of NHS termination services meets national guidance and women's needs.

- 2.81 Secondly, it has been suggested that the introduction of NIPT will lead to less demand for invasive diagnostic testing services, such as amniocentesis and CVS: the RAPID study predicts that over 3,000 fewer diagnostic tests will be carried out each year. Respondents to our consultation suggested that this could lead to a de-skilling of healthcare professionals (although it should be noted that diagnostic testing is used for purposes other than diagnosing Down's, Edwards' and Patau's syndromes). Diagnostic testing requires experience on the part of the healthcare professional carrying out the procedure, and there is evidence to suggest that operators who perform procedures frequently have lower miscarriage rates.²⁵⁶ Women may only be able to access diagnostic testing at specialist centres in future.²⁵⁷ Conversely, it has been suggested that increased uptake of NIPT in the private sector may increase demand for diagnostic testing. Several private providers of NIPT offer to test fetuses for genetic variations, such as microdeletions and sex aneuploidies, in addition to testing for Down's, Edwards' and Patau's syndromes. These tests have higher rates of false positive results, which could lead more women to seek support and unnecessary diagnostic testing in the NHS (see Paragraphs 1.28-1.29).
- 2.82 Thirdly, NHS healthcare professionals will need to consider how unanticipated or secondary findings from NIPT will be dealt with. Such findings could include clinically relevant genetic information about the pregnant woman and maternal cancerous and malignant tumours.²⁵⁸ The possibility of these kinds of findings exists only when particular laboratory and processing methods are used. Some NIPT manufacturers use technology that masks any findings other than those requested by the pregnant woman. Others usually inform the woman's doctor of any unanticipated or secondary findings and allow the doctor to make a judgment about whether to inform the woman.²⁵⁹ The American College of Medical Genetics and Genomics (ACMG) recommends informing women before testing of the possibility of identifying maternal genomic anomalies and that this possibility depends on the specific methodology used, and that women should be referred to a trained genetics professional when NIPT identifies such anomalies.²⁶⁰ Respondents to the consultation were concerned that the potential for unanticipated or secondary findings could raise significant issues for healthcare professionals. There are

²⁵⁵ Robson SC, Kelly T, Howel D *et al.* (2009) Randomised preference trial of medical versus surgical termination of pregnancy less than 14 weeks' gestation (TOPS) *Health Technology Assessment* **13**: 1-124, iii-iv.

²⁵⁶ Royal College of Obstetricians and Gynaecologists (2010) *Green-top guideline no. 8. amniocentesis and chorionic villus sampling*, available at: https://www.rcog.org.uk/globalassets/documents/guidelines/gtg_8.pdf.

²⁵⁷ Royal College of Obstetricians and Gynaecologists (2014) *Non-invasive prenatal testing for chromosomal abnormality using maternal plasma DNA. Scientific impact paper No. 15*, available at: https://www.rcog.org.uk/globalassets/documents/guidelines/sip_15_04032014.pdf.

²⁵⁸ Bianchi DW, Chudova D, Sehnert AJ *et al.* (2015) Noninvasive Prenatal Testing and Incidental Detection of Occult Maternal Malignancies *Jama* **314**: 162-9.

²⁵⁹ Personal communication with NIPT manufacturers.

²⁶⁰ Gregg AR, Skotko BG, Benkendorf JL *et al.* (2016) Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics *Genetics in Medicine* **18**: 1056-65.

calls for more research on patients' experiences to inform best practice for consent and, where relevant, feedback to patients.²⁶¹

- 2.83 Fourthly, NIPT might be perceived to present ethical issues for NHS healthcare professionals who believe that integrating NIPT into NHS prenatal screening could increase the number of terminations of pregnancies, or contribute to negative societal attitudes towards people with Down's, Edwards' and Patau's syndromes. This might exacerbate existing challenges for healthcare professionals who have conscientious objections to prenatal screening. Some of our survey and consultation respondents raised concerns about this:

"There is an argument that some may not wish to facilitate a technique that may lead to more women choosing to abort fetuses with a trisomy." (Person with multiple interests in NIPT – survey respondent²⁶²)

"Prenatal screening has been imposed on many professionals who do not hold with its principles, introducing NIPT may simply increase the problems that the imposition brings." (Saving Down Syndrome – consultation respondent)

- 2.84 Doctors are able to practice medicine in accordance with their personal beliefs, and can conscientiously object to, and opt out of providing, a test or treatment, as long as a number of other conditions are met. These include that doctors tell patients about their right to see another doctor who does not hold the same objection, ensure that their patient has enough information to exercise their right to see another practitioner, and that opting out of providing a test or treatment for a patient does not result in discrimination.²⁶³ Nurses and midwives are able to make conscientious objections to tests and treatments in limited circumstances, which are direct participation in the process of treatment involved in abortion and in treatment involving technological assisted conception practices.²⁶⁴ There remains uncertainty about the implications of the introduction of NIPT on the NHS, and therefore it is unclear whether NIPT will present any distinctive or novel problems for NHS healthcare professionals who have ethical objections to prenatal screening and termination.
- 2.85 Finally, there is the question of how the NHS will meet the demand for NIPT laboratory services. The samples collected during the RAPID study were tested at an NHS genetics laboratory using a protocol that was developed and validated in-house for the study. If NIPT is rolled out as a second stage test across the UK, it is predicted that approximately 7,700 tests will need to be carried out each year.²⁶⁵ These tests will need to be carried out at a cost of £250 per test or less if the cost calculations of the RAPID study are to hold. We are aware that Public Health England is currently considering how testing will be carried out once NIPT is offered as a service in the NHS. There are several intellectual property disputes between NIPT companies that are currently ongoing, which could have an impact on how and whether private companies are commissioned by the NHS to provide NIPT services. International guidance says that licensing practices should not

²⁶¹ Dheensa S, Shkedi-Rafid S, Crawford G *et al.* (2016) Management of incidental findings in clinical genomic sequencing studies, in *eLS* (Wiley Online Library).

²⁶² Survey respondent with experience of undergoing NIPT and a general professional interest in prenatal testing.

²⁶³ General Medical Council (2013) *Personal beliefs and medical practice*, available at: http://www.gmc-uk.org/static/documents/content/Personal_beliefs-web.pdf.

²⁶⁴ Nursing and Midwifery Council (2015) *The code: professional standards of practice and behaviour for nurses and midwives*, available at: <https://www.nmc.org.uk/globalassets/sitedocuments/nmc-publications/nmc-code.pdf>.

²⁶⁵ Chitty LS, Wright D, Hill M *et al.* (2016) Uptake, outcomes, and costs of implementing non-invasive prenatal testing for Down's syndrome into NHS maternity care: prospective cohort study in eight diverse maternity units *British Medical Journal* **354**: i3426.

be used to restrict the choice of other products or services by patients and their healthcare providers.²⁶⁶

Future NHS prenatal screening programmes

2.86 The proposal to offer NIPT to women as part of the NHS prenatal screening programme has ignited a public debate about whether screening fetuses for Down's syndrome should happen at all. A number of people who responded to the survey and consultation raised concerns about the aims of Down's syndrome screening and whether it would today meet the criteria for new screening programmes used by the UK National Screening Committee (UKNSC). In addition, the fast pace of research on NIPT means that it is possible that NIPT for more genetic conditions, or whole 'panels' of genetic conditions, will become candidates for future prenatal screening programmes that will need assessment by the UKNSC.²⁶⁷ Given recent calls on governments and public health authorities to adopt an active role to ensure the responsible innovation of prenatal screening on the basis of ethical principles where prenatal screening is offered as a public health programme,²⁶⁸ we believe an examination of the aims of and criteria for NHS prenatal screening programmes where termination of pregnancy is an option to be timely.

Aims and outcomes of prenatal screening

2.87 The aim of NHS screening programmes is "to identify apparently healthy people who may be at increased risk of a disease or condition, enabling earlier treatment and better informed decisions". The NHS fetal anomaly screening programme aims to "ensure there is equal access to uniform and quality-assured screening across England and women are provided with high quality information so they can make an informed choice about their screening and pregnancy options."²⁶⁹ Similarly, the aim of fetal anomaly and Down's syndrome screening in Scotland is "to offer fetal anomaly screening to all pregnant women in Scotland to provide them with information, which allows them to make informed choices."²⁷⁰ These broad aims could be thought to include the sub-aims of: providing reassurance to pregnant women and couples, giving potential parents the opportunity to prepare for the birth of a disabled child, enabling interventions during pregnancy and birth that may improve the prospects for a disabled baby, and giving pregnant women the choice not to have a disabled child by having a termination. The aim of fetal anomaly screening to promote informed choice in pregnancy is not an aim to promote unlimited choice: it is to promote choice relating to information about significant medical conditions and impairments.

²⁶⁶ Organisation for Economic Co-operation and Development (2006) *Guidelines for the licencing of genetic innovations*, available at: <https://www.oecd.org/sti/biotech/36198812.pdf>.

²⁶⁷ Boardman FK, Young PJ and Griffiths FE (2017) Population screening for spinal muscular atrophy: A mixed methods study of the views of affected families *American Journal of Medical Genetics Part A*: 421-34.

²⁶⁸ Dondorp W, de Wert G, Bombard Y *et al.* (2015) Non-invasive prenatal testing for aneuploidy and beyond: challenges of responsible innovation in prenatal screening *European Journal of Human Genetics* **23**: 1438-50.

²⁶⁹ NHS England (April 2015) *Fetal anomaly screening programme handbook for ultrasound practitioners*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/443865/FASP_ultrasound_handbook_July_2015_090715.pdf.

²⁷⁰ NHS Scotland (2015) *National protocols: fetal anomaly and Down's syndrome screening* available at: <http://www.nsd.scot.nhs.uk/Documents/2015%20-%20Fetal%20Anomaly%20and%20Down's%20Syndrome%20Screening%20Protocols%20-%20v%201.pdf>.

- 2.88 Some respondents to the survey and consultation were concerned that the aim of the Down's syndrome screening programme is to reduce or eradicate people with Down's syndrome in order to improve public health, reduce the burden on state resources or reduce costs, and that this is a form of eugenics (see Paragraphs 2.70-2.75). Historically, reducing the incidence of Down's syndrome is likely to have been an objective of prenatal screening,²⁷¹ and it is possible that some people still support this aim. The idea that public health policies should not aim to reduce the incidence of disability through screening has also been challenged.²⁷² However, today, the recognised equal rights of disabled people and the duty to support disabled people mean that reducing or eradicating disabled people cannot be an explicit aim of prenatal screening.²⁷³

"Well it does feel, especially in the current political and social climate, a little bit like an attempt to eradicate disabled people." (Person with a genetic condition – interviewee)

- 2.89 Regardless of the aim, prenatal screening where termination is an option may have consequences, intended or otherwise, that include a reduction in the number of people living with the condition. Other possible consequences include an increase in anxiety for women receiving high chance results. NIPT is sometimes misrepresented in the media as a safe equivalent to diagnostic procedures, with a focus on high detection rates, and so women may have incorrect or incomplete knowledge of its capabilities.²⁷⁴ Therefore, high levels of anxiety might be expected in women in response to a high chance NIPT result, similar to those experienced by women receiving a positive diagnosis via amniocentesis. Recognising that there may be consequences of prenatal screening beyond those being aimed for, is important for the appraisal of the appropriateness of screening programmes.
- 2.90 Measuring whether prenatal screening programmes have been successful in meeting their aims is important for informing reviews of existing programmes and decisions about new programmes. NHS Service Specification 16 states that the expected health outcomes of prenatal screening for Down's, Edwards' and Patau's syndromes are that women are able to make informed and supported decisions about the risk calculation given within the screening programme, and that diagnostic and follow-on care services are easily accessible and support a woman's decision. NICE Quality Statement 10 within the Antenatal Care Quality Standards for England suggests the outcome measures for the national fetal anomaly screening programme should include that pregnant women feel they have made an informed decision about whether to undergo fetal anomaly screening.²⁷⁵ However, there is currently no clinically appropriate measure of informed choice.
- 2.91 The standards against which the delivery of NHS fetal anomaly screening programme is measured include: that every eligible pregnant woman is offered screening; the test performs well; results are reported quickly; and that women with screen-positive results are offered a timely opportunity to discuss the results and further options.²⁷⁶ Direct

²⁷¹ See, for example: Wald NJ, Cuckle HS, Densem JW *et al.* (1988) Maternal serum screening for Down's syndrome in early pregnancy *British Medical Journal* **297**: 883-7.

²⁷² Wilkinson S (2015) Prenatal screening, reproductive choice, and public health *Bioethics* **29**: 26-35.

²⁷³ Iltis AS (2016) Prenatal screening and prenatal diagnosis: contemporary practices in light of the past *Journal of Medical Ethics* **42**: 334-9.

²⁷⁴ Lewis C, Choudhury M and Chitty LS (2015) 'Hope for safe prenatal gene tests'. A content analysis of how the UK press media are reporting advances in non-invasive prenatal testing *Prenatal diagnosis* **35**: 420-7.

²⁷⁵ National Institute for Health and Clinical Excellence (2016) *Quality statement 10: Screening – national fetal anomaly screening programmes*, available at: <https://www.nice.org.uk/guidance/QS22/chapter/Quality-statement-10-Screening-national-fetal-anomaly-screening-programmes>.

²⁷⁶ Public Health England (2015) *Fetal anomaly screening programme standards 2015-16*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/421650/FASP_Standards_April_2015_final_2_.pdf.

assessment of the extent to which women have made informed choices about whether to have screening or not is not included in the standards due to the difficulty of measuring such a complex process. However, it is known that uptake of Down's syndrome screening is highly variable across hospital trusts and in different parts of the country, which suggests that the extent to which women make informed choices varies in different areas. A better understanding of the factors at work would be helpful for ensuring women have access to the information and support they need to make informed choices.

Criteria for prenatal screening

2.92 Some respondents to our survey and consultation suggested that several of the UKNSC's criteria for appraising the viability, effectiveness and appropriateness of screening programmes are inappropriate or unclear in the context of prenatal screening where termination of pregnancy is an option (in England, Wales and Scotland; termination on the grounds of fetal anomaly is illegal in Northern Ireland). Some examples of criticisms of the criteria and how they are used to evaluate screening programmes are given below.

- **Criteria 1. "The condition should be an important health problem as judged by its frequency and/or severity."** It is not clear how conditions that manifest in uncertain or highly variable ways are judged, and whether this includes or excludes adult onset conditions, which are likely to be ineligible for prenatal screening.
- **Criteria 9. "There should be an effective intervention for patients identified through screening with evidence that intervention at a pre-symptomatic phase leads to better outcomes for the screened individual compared with usual care."** It is not clear who the patient is in the context of prenatal screening. Legally, the woman is the patient in pregnancy, but in some cases screening may be offered in order to improve outcomes for the fetus or future person. In terms of 'effective interventions', prenatal screening is different to adult screening when termination of pregnancy is one of the interventions available to individuals with a positive diagnosis. Enabling women to exercise their reproductive autonomy regarding termination has other consequences. Although few women report feelings of regret about a decision to have a termination following a diagnosis of fetal anomaly, such a decision is frequently described by pregnant women and couples as painful and distressing, which is not taken into account in current assessments. The criteria also do not specify whether the effective intervention must be one that is carried out prenatally, during birth or soon after birth. If the available intervention can be carried out during childhood or later, then there would be no need to screen prenatally for the condition. In addition, assessing whether a 'better outcome' is likely to be achieved following a termination of pregnancy would be difficult.
- **Criteria 12. "There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/intervention) is clinically, socially and ethically acceptable to health professionals and the public."** Assessing the ethical and social issues is particularly important in the case of prenatal screening programmes, given that the screening programme may lead to more terminations, and these might result in a reduction in the incidence or prevalence of people with the condition being screened for. However, aiming to demonstrate that a screening programme is 'ethically acceptable' to the public is likely to be challenging. Given the range of views that tend to exist on prenatal screening programmes, a consensus is not likely to be possible, and a majority judgment is unlikely to be acceptable to

everyone. More important is an assessment of the ethical issues and how tensions between them might best be resolved (as we are attempting to do in this report). A 2015 review of the UKNSC made recommendations for improving the way in which social, ethical, and legal issues associated with screening are considered. These included seeking expert input from established groups and making explicit the processes or expertise it has drawn on in reaching conclusions about social, ethical and legal issues.²⁷⁷

■ **Criteria 14. “The opportunity cost of the screening programme should be economically balanced in relation to expenditure on medical care as a whole.”**

The cost of screening and the fair allocation of state resources clearly need to be considered. However, the cost of care of people with the condition being screened for should not enter into the equation for prenatal screening programmes, given that reducing the number of or eradicating disabled people in order to improve public health and reduce the burden on state resources cannot be a legitimate aim of prenatal screening (see Paragraph 2.88). This is not clear in the existing criteria.

- 2.93 A further criticism of the criteria was that they do not appear to take into consideration the potential effects of screening programmes on people with the conditions being screened for (see Paragraphs 2.53-2.76). The Public Sector Equality Duty imposes responsibilities on public service providers such as the UKNSC to consider all individuals when carrying out their day-to-day work, including shaping policy and delivering services. It requires that public bodies have due regard to the needs to eliminate discrimination, advance equality of opportunity and foster good relations between different people when carrying out their activities.²⁷⁸ In addition, the potential effects of screening programmes on the future child or person are not considered by the criteria. Such effects would be particularly relevant if whole genome or exome sequencing using NIPT was ever to be considered by the UKNSC for a screening programme in the future.
- 2.94 There is a lack of transparency regarding the process of appraising screening programmes. For example, there is no publicly available analysis of how NIPT for Down's, Edwards' and Patau's syndromes was assessed against the criteria by the UKNSC in order to reach its decision, nor a summary or analysis of the responses received to its public consultation. Yet the 2015 review of the UKNSC recommended that it should be clear how evidence from stakeholders had been considered.
- 2.95 Screening programmes that have been approved are periodically reviewed by the UKNSC to ensure that they still meet the criteria. The factors that affect whether a prenatal screening programme meets the criteria can change over time, such as the cost or performance of the test, the availability of prenatal *in utero* treatment, the health and social prospects of people with the condition and public attitudes towards the screening programme. Again, it is not explicit or transparent how and when reviews of existing programmes take place.

²⁷⁷ UK National Screening Committee (2015) *Review of the UK National Screening Committee (UK NSC)*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/443953/20150602_-_Final_Recommendations.pdf.

²⁷⁸ See Government Equalities Office and Equality and Human Rights Commission (2015) *Equality Act 2010: guidance*, available at: <https://www.gov.uk/guidance/equality-act-2010-guidance#public-sector-equality-duty>.

Chapter 3

NIPT for rare genetic
conditions in the NHS

Chapter 3 – NIPT for rare genetic conditions in the NHS

Chapter overview

Non-invasive prenatal testing (NIPT) can be used to test fetuses for rare *de novo* genetic conditions, such as thanatophoric dysplasia, and certain inherited genetic conditions, such as cystic fibrosis. In some cases, NIPT is diagnostic and removes the need for invasive testing. Pregnant women and couples are usually referred by their obstetrician, midwife or GP to a specialist NHS genetic testing service for this kind of prenatal testing.

Decisions about what tests should be offered and to which patients are made on a case-by-case basis by doctors such as clinical geneticists. The UK Genetic Testing Network evaluates the scientific validity and clinical utility of new genetic tests that its member laboratories would like to offer NHS patients. Tests from non-NHS, including non-UK, laboratories can also be requested by the genetics team.

Healthcare professionals involved in the delivery of prenatal genetic testing services are appropriately trained, and information is given in a timely and non-directive fashion. Genetic counsellors and nurses are widely recognised as an integral parts of the multidisciplinary team.

The availability of NIPT for rare genetic conditions in the NHS is still quite limited. As NIPT becomes more widely available, and if the number of prenatal diagnoses increases in the future, this might reinforce or amplify negative messages about the societal value placed on people with genetic conditions. Prenatal testing can have benefits for people with genetic conditions by enabling them to make informed choices in pregnancy.

NIPT for further genetic conditions, or 'panel tests' for several related conditions, are likely to be developed for NHS use in future. NIPT for adult onset conditions or carrier status may also become available. Arguments for not genetically testing a child in order to respect the autonomy and interests of the future adult also apply to not testing a fetus for adult onset conditions in a continuing pregnancy. Testing a fetus for carrier status generally has no immediate clinical use, and may undermine the autonomy and interests of the future person.

Whole genome and exome sequencing of fetuses using NIPT might become available in the future. Revealing information about the fetus that is of unknown or uncertain clinical significance could create unnecessary anxiety and lead more women to have invasive diagnostic procedures. This information would also have limited clinical utility, and may be harmful to the person that the fetus may become if it is stored and analysed later.

Introduction

- 3.1 There are many other genetic conditions in addition to Down's, Edwards' and Patau's syndromes that can arise at the time of conception (such as thanatophoric dysplasia), but these tend to be much rarer and are not individually screened for in pregnancy by the NHS. However, the ultrasound scan that is offered to all pregnant women at 18-20 weeks checks the physical development of the fetus and, if anomalies are found that indicate a possible genetic condition, the woman may be referred to NHS genetic testing services. Previously, genetic testing usually involved an invasive diagnostic procedure such as amniocentesis or chorionic villus sampling (CVS). Recently, non-invasive prenatal testing (NIPT) techniques have been used to develop non-invasive tests for some rare *de novo* genetic conditions. Several of these tests are diagnostic and remove the need for invasive testing altogether.
- 3.2 Some genetic conditions can be present in families across generations, such as cystic fibrosis and Duchenne muscular dystrophy. Women and couples with a family history of a genetic condition have a number of options available to them if they wish to avoid their biological children inheriting the condition. One option is to conceive naturally and perform genetic testing on the fetus once this is possible (this varies depending on the procedure). Again, previously, genetic testing usually involved an invasive diagnostic procedure such as amniocentesis or CVS. Now, the availability of NIPT for some inherited genetic conditions means that women can have a non-invasive test, and in some cases this provides a definitive diagnosis and there is no need for the woman to have invasive testing. Another option for couples is to conceive using *in vitro* fertilisation (IVF) and make use of preimplantation genetic diagnosis (PGD) of the resulting embryos, although this is not usually the first choice given IVF can be a stressful and unpleasant process and is often unsuccessful.
- 3.3 The objective of this kind of genetic testing has been defined as “to provide prenatal diagnostic testing services (for genetic conditions) that enable families to make informed choices, consistent with their individual needs and values and to support them in dealing with the outcome of such testing”.²⁷⁹

Current availability and regulation

- 3.4 The NHS service specification for medical genetics covers the diagnostic and genetic counselling services provided by clinical genetics departments to patients affected by or with the chance of having a genetic condition. The principal objective of the clinical genetics service is to provide “integrated clinical and laboratory genetic services that are equitable, safe, efficient, appropriate, accessible and acceptable to all sectors of the community and of a demonstrably high quality.”²⁸⁰ There are 23 NHS regional genetics centres in the UK, all with strong links to genetics laboratories, general medical specialties and their clinical networks.²⁸¹

²⁷⁹ Skirton H, Goldsmith L, Jackson L, Lewis C and Chitty L (2014) Offering prenatal diagnostic tests: European guidelines for clinical practice *European Journal of Human Genetics* **22**: 580-6.

²⁸⁰ NHS England (2013) *Service Specification E01/S/a: medical genetics (all ages)*, available at: <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2014/04/e01-med-gen.pdf>.

²⁸¹ UK Genetic Testing Network (2015) *NHS genetic services: The UK catalogue*, available at: http://ukgtn.nhs.uk/fileadmin/uploads/ukgtn/Documents/Resources/Library/Reports_Guidelines/NHS_Genetic_Services_The_UK_Catalogue.pdf.

3.5 The UK Genetic Testing Network (UKGTN) evaluates the scientific validity and clinical utility of new genetic tests that its member laboratories would like to offer NHS patients. The UKGTN evaluates genetic tests for rare disorders, that it defines as those usually affecting fewer than 1 in 2,000 individuals. The evaluation takes into account the seriousness and prevalence of the condition, the purpose, performance, clinical utility and price of the test and any ethical, legal and social considerations.²⁸² There are no formal guidelines publicly available, but the UKGTN takes the following factors into account in the assessment of new tests:

- the evidence for the analytical, scientific and clinical validity and the performance of the test;
- whether the test alerts significant clinical co-morbidities, reduces mortality or saves lives, avoids irreversible harm, avoids diagnostic procedures or tests (some of which may be invasive) and/or multiple hospital appointments, avoids incorrect management that could be harmful, and confirms targeted therapy or management;
- whether the test enables earlier diagnosis allowing commencement of treatment earlier with associated improved prognosis, enables access to educational and social support, enables at-risk family members that test negative for a familial mutation to be discharged from follow-up, and enables at-risk family members that test positive for a familial mutation to have appropriate follow-up.²⁸³

The evaluation is carried out by a multi-disciplinary committee that includes clinicians, clinical scientists, a patient organisation representative and professional advisors (medical, scientific and public health). Once a test has been approved, it is entered into the NHS Directory of Genetic Disorders/Genes for Diagnostic Testing, and testing criteria are developed that outline the clinical indications for when testing would be appropriate. Laboratories must be able to offer any UKGTN-approved tests nationally.

3.6 The UKGTN has approved NIPT tests for a number of single gene conditions. For each test, a clinical care pathway has been developed that outlines how the test should be offered and delivered.²⁸⁴ All of the NIPT tests that have been approved are diagnostic, can be carried out from nine weeks of pregnancy, and are for conditions for which genetic testing is already taking place in the NHS. These include:

- Cystic fibrosis – couples who are both carriers of a genetic mutation that causes cystic fibrosis have a 25 per cent chance of having a child with the condition. NIPT can be carried out when both parents are known carriers of one of these genetic mutations and the father has a different mutation to the mother, which is the case in around 30 per cent of couples with the chance of having a child with cystic fibrosis. Cystic fibrosis affects around 1 in every 2400 live births.²⁸⁵
- Apert syndrome – Apert syndrome usually occurs as a new event (*de novo*) in a family, and there is a very small chance of recurrence. Someone with Apert syndrome has a 50 per cent chance of their children inheriting the condition. NIPT can be used to

²⁸² UK Genetic Testing Network (2016) *Evaluation of new genetic tests for NHS services September 2016* available at: http://ukgtn.nhs.uk/fileadmin/uploads/ukgtn/Documents/Resources/Library/Reports_Guidelines/Briefing_Report_Gene_Test_RecommendationsTO_CSAG_SEPT16.pdf.

²⁸³ Personal communication with UKGTN.

²⁸⁴ See for example: UK Genetic Testing Network (2010) Best practice guidelines for non-invasive prenatal diagnosis to determine fetal sex for known carriers for X linked conditions excluding haemophilia, available at: <https://ukgtn.nhs.uk/fileadmin/uploads/ukgtn/Documents/Resources/Library/NIPD/BPCAREPATWAYSNIPTX-LinkedConditionsFINAL.pdf>.

²⁸⁵ UK Genetic Testing Network (2014) *Gene dossier: cystic fibrosis*, available at: http://ukgtn.nhs.uk/uploads/tx_ukgtn/CF_CFTR_NIPD_GD_Sept14.pdf.

diagnose Apert syndrome in a fetus when it has occurred as a *de novo* event or when the father is affected. Apert syndrome affects around 1 in 100,000 live births.²⁸⁶

- X-linked conditions – some genetic conditions are linked to the X chromosome, such as Duchenne muscular dystrophy (DMD), and affect mainly boys. The sons of women who are carriers of DMD have a 50 per cent risk of being affected by the condition; while their daughters may also inherit the altered gene, their chance of developing the condition is very small. If NIPT determines that the fetus is female, no further testing is necessary. If the fetus is male, diagnostic testing may be offered. DMD affects around 1 in every 4000 male live births.²⁸⁷
 - Skeletal disorders caused by mutations in the FGFR3 gene – including achondroplasia (which affects 5-15 in 100,000 live births) and thanatophoric dysplasia (which affects 2-3 in 100,000 live births). Most babies with thanatophoric dysplasia die in the first hours or days of life. Both conditions can occur *de novo*, and there is a very small chance of recurrence. NIPT can be used to distinguish between achondroplasia and thanatophoric dysplasia and when a previous pregnancy has been affected. Where one parent or both parents has achondroplasia the chance of having a child with the condition is 50 per cent. Where both parents have achondroplasia there is also a 25 per cent chance of having a child who will be stillborn or die soon after birth. NIPT can also be used to test for achondroplasia when the father has the condition.²⁸⁸
 - Craniosynostosis syndromes caused by mutations in the FGFR2 gene – including Antley-Bixler syndrome, Crouzon syndrome, Jackson-Weiss syndrome and Pfeiffer syndrome. These are dominant conditions, with an overall incidence of 1 in every 2000-2500 live births. NIPT can be used to test for these conditions when they arise *de novo*, when a previous pregnancy has been affected, and when the father has the condition (and so there is a 50 per cent chance the fetus will be affected).²⁸⁹
- 3.7 Once a test has been approved, it is recommended to be considered for NHS funding. Each country in the UK follows its own process for considering adoption of the tests and, as far as we are aware, all of the NIPT tests that have been approved by the UKGTN have been approved for NHS funding in each country. However, as services are commissioned locally, there is no guarantee an approval will automatically lead to funding of this test across the country as a whole.
- 3.8 The UKGTN process focuses on the tests provided by NHS laboratories, rather than the clinical genetics centres that arrange or request genetic tests for patients. Genetics centres can access genetic tests that are not approved by the UKGTN, such as tests offered on a local basis, tests offered by NHS laboratories that are not members of the UKGTN, and tests offered by laboratories based outside of the NHS or the UK, if this is judged to be appropriate by the genetics team.

²⁸⁶ UK Genetic Testing Network (2014) *Gene dossier: Apert syndrome*, available at: http://ukgtn.nhs.uk/uploads/tx_ukgtn/Apert_Syndrome_FGFR2_NIPD_GD_Sept14.pdf.

²⁸⁷ UK Genetic Testing Network (2011) *Gene dossier: fetal sexing by non invasive prenatal diagnosis for serious X-linked conditions*, available at: https://ukgtn.nhs.uk/uploads/tx_ukgtn/NIPDXlinkedexhaemManchester.pdf.

²⁸⁸ UK Genetic Testing Network (2013) *Gene dossier: skeletal disorders caused by mutations in the FGFR3 gene*, available at: https://ukgtn.nhs.uk/uploads/tx_ukgtn/FGFR3_Related_Skeletal_Dysplasia_Panel_Test_NIPD_GD_Sept_13_1.pdf

²⁸⁹ UK Genetic Testing Network (2015) *Gene dossier: FGFR2-related craniosynostosis syndromes*, available at: https://ukgtn.nhs.uk/uploads/tx_ukgtn/FGFR2_NIPD_GD_Sept_15.pdf.

- 3.9 There are no UK-specific guidelines for healthcare professionals on NIPT offered through specialist genetics testing services. European guidelines for health professionals who are involved in prenatal diagnosis were published in 2014 by EuroGentest, a project funded by the European Commission to harmonise the process of genetic testing across Europe. The focus of the project was prenatal diagnosis for women who have an increased chance of having a fetus with a specific condition, rather than genetic screening of whole populations. The guidelines aim to provide a flexible framework for ethical clinical care and describe general principles, logistical considerations, clinical care and counselling topics in the context of prenatal diagnosis.²⁹⁰
- 3.10 NIPT also can be used to determine whether a pregnant woman with a rhesus D negative blood type requires medication to prevent haemolytic disease in the fetus. If, through NIPT, the fetus is found to also have a rhesus negative blood type, no medication is required. The National Institute for Health and Care Excellence (NICE) has published guidance on the use of NIPT for fetal rhesus D genotype in pregnant women. The guidance is not binding but NHS commissioners and providers are expected to take it “fully into account”.²⁹¹
- 3.11 Other than the UK Medical Devices Regulations 2002, from which genetic tests that are manufactured and used by NHS hospitals and laboratories generally are exempt, there are no laws or regulations that apply to NIPT tests offered within the NHS.²⁹² This contrasts with the regulation of PGD, which restricts the treatment purposes for which PGD can be used and prohibits selecting embryos for sex for social reasons (see Paragraph 1.37).
- 3.12 NIPT of fetuses for conditions that pregnant women have themselves is in the research phase.²⁹³ In these cases, the woman will have the altered gene present in her blood and it is difficult for NIPT to distinguish the genes of the woman from those of the fetus. NIPT for conditions caused by microdeletions and sex chromosome aneuploidy, which is available in the private sector (see Paragraphs 1.28-1.29), is not currently available in the NHS.

Implications of NIPT for rare genetic conditions in the NHS

Test safety and performance

- 3.13 For some rare genetic conditions, NIPT is diagnostic. The availability of diagnostic NIPT in the NHS removes the need for women to have invasive diagnostic testing which carries a small risk of miscarriage (see Paragraph 1.10) and is unpleasant for the woman. For other rare genetic conditions, such as those linked to the sex of the fetus, NIPT is not

²⁹⁰ Skirton H, Goldsmith L, Jackson L, Lewis C and Chitty L (2014) Offering prenatal diagnostic tests: European guidelines for clinical practice *European Journal of Human Genetics* **22**: 580-6.

²⁹¹ National Institute for Health and Clinical Excellence (2016) *Diagnostics guidance. High-throughput non-invasive prenatal testing for fetal RHD genotype* available at: <https://www.nice.org.uk/guidance/dg25/resources/highthroughput-noninvasive-prenatal-testing-for-fetal-rhd-genotype-1053691935685>.

²⁹² Part IV of the Medical Devices Regulations 2002, available at <http://www.legislation.gov.uk/uksi/2002/618/part/IV/made>.

²⁹³ Lun FM, Tsui NB, Chan KC *et al.* (2008) Noninvasive prenatal diagnosis of monogenic diseases by digital size selection and relative mutation dosage on DNA in maternal plasma *Proceedings of the National Academy of Sciences of the United States of America* **105**: 19920-5; Tsui NB, Kadir RA, Chan KC *et al.* (2011) Noninvasive prenatal diagnosis of hemophilia by microfluidics digital PCR analysis of maternal plasma DNA *Blood Journal* **117**: 3684-91; Hui WW, Jiang P, Tong YK *et al.* (2017) Universal haplotype-based noninvasive prenatal testing for single gene diseases *Clinical chemistry* **63**: 513-24; New MI, Tong YK, Yuen T *et al.* (2014) Noninvasive prenatal diagnosis of congenital adrenal hyperplasia using cell-free fetal DNA in maternal plasma *The Journal of Clinical Endocrinology and Metabolism* **99**: E1022-30.

diagnostic but provides a first stage test that reduces the number of women who might go on to have diagnostic testing.

- 3.14 NIPT for rare genetic conditions can be carried out in twin or multiple pregnancies. If the twins share a placenta, as in the case of identical twins, NIPT will determine if both or neither twin has the condition being tested for. If the twins have separate placentas, NIPT will determine if neither twin has the condition, but if the condition is detected, a diagnostic test or ultrasound will be necessary to find out if one or both twins are affected if the parents wish to know this information.

Access

- 3.15 Pregnant women are usually referred to a genetic testing service by their obstetrician, midwife or GP. This may be in advance of a pregnancy if a couple knows that any child they have will have a chance of a genetic condition. This may be because one of the parents is affected by a genetic condition, they have already had an affected child, or because they have a family history of the condition. A referral may also arise in the course of a pregnancy if problems are identified on an ultrasound scan, because of problems with maternal health, or if the couple becomes aware of a potentially relevant family history. Therefore, the two major groups of referred women and couples are those who already have a good knowledge of the condition in advance of having to make a decision, and those who are forced to make a decision very quickly under difficult circumstances. Decisions about what tests should be offered and to which patients are made on a case-by-case basis by doctors such as clinical geneticists. If a test that has been approved by the UKGTN is being used, clinicians are guided in their decisions by testing criteria that are developed by the UKGTN. The criteria set out the circumstances in which testing should take place, such as the gestation of the pregnancy and the carrier status of the couple.
- 3.16 Access to NIPT enables women with a family history of some conditions to find out if their fetus is affected significantly earlier than before. Currently, prenatal genetic testing usually involves an invasive diagnostic procedure such as amniocentesis or CVS. CVS can be carried out from eleven weeks and amniocentesis can be carried out from 15 weeks. Now, the availability of NIPT for some inherited genetic conditions means women can have a non-invasive test from approximately nine weeks of pregnancy. This may be advantageous, particularly for women considering a termination.

Provision of information and support

- 3.17 Pregnant women and couples who have been referred for genetic testing, including NIPT, are talked through the process by specialists such as clinical geneticists, specialist genetic nurses and non-medical genetic counsellors. The EuroGentest guidelines make recommendations related to the information and support that should be offered to women and couples undergoing any kind of prenatal diagnosis, including:
- Healthcare professionals involved in offering prenatal diagnosis must ensure they are informed and maintain their knowledge on all relevant aspects of prenatal diagnosis.
 - Prenatal genetic diagnosis is offered as a choice to prospective parents; there should be no element of pressure or coercion involved.
 - Pre- and post-test counselling should be available and carried out by appropriately trained professionals.

- Professionals should ensure prospective parents are able to make an informed choice through the provision of accurate, balanced information in a clearly understandable form.
- When the pregnancy continues after testing and the child is affected, suitable arrangements should be made for the ongoing management of the pregnancy and care of the child after birth in consultation with the relevant neonatal/paediatric teams.²⁹⁴

3.18 The Joint Committee on Genomics in Medicine (JCGM) (formerly the Joint Committee on Medical Genetics), which is a joint committee of the Royal College of Physicians, Royal College of Pathologists and the British Society for Genetic Medicine, has published guidance on consent and confidentiality in the context of genetic testing. The most recent guidance published in 2011 includes recommendations on seeking consent and, in particular, on communicating to patients the potential relevance of the results of genetic testing for other family members. The guidance also recommends the possibility of unexpected or incidental findings from genetic testing, and the routine practice of long-term storage of samples for possible future analysis, should be discussed as part of the consent process.²⁹⁵ The JCGM is in the process of updating this guidance.

3.19 In the responses to our survey and consultation, we received generally positive feedback about the information and support that is provided in practice to women and couples undergoing NIPT for rare genetic conditions. Women and couples are often already well informed about the condition if they have the condition themselves or it is in their family. Healthcare professionals involved in the delivery of prenatal genetic testing services tend to be appropriately skilled, and information is given in a timely and non-directive fashion. However, we did hear some reports of women being directed towards termination and a tendency for the focus to be on medical problems associated with the condition rather than information about day-to-day life.

"I think he [fetal medicine specialist] did his best to tell us what he thought we needed to know. Yes, and he was really lovely afterwards. Everyone was really lovely, actually. We didn't have any negative experiences afterwards." (Woman with experience of undergoing NIPT - interviewee)

"We got that information and it paints a really, really bleak picture, I think, of life and what life can be like." (Woman with experience of undergoing NIPT - interviewee)

"So, the first consultant, who made the diagnosis... There was definitely a presumption that we would terminate." (Woman with experience of undergoing NIPT - interviewee)

3.20 The provision of accurate, balanced and non-directive information and the need for sufficient time to discuss any questions and concerns may become even more important as NIPT for rare genetic conditions becomes more widely available. As with NIPT in wider screening programmes, consultation respondents suggested that the lack of risk to the fetus posed by NIPT for rare genetic conditions could mean that women feel that they are expected to have NIPT, or that there is no reason not to. There is a risk that NIPT might be seen as 'just a blood test' and that women will not give NIPT the same level of consideration that they would an amniocentesis or CVS procedure.

²⁹⁴ Skirton H, Goldsmith L, Jackson L, Lewis C and Chitty L (2014) Offering prenatal diagnostic tests: European guidelines for clinical practice *European Journal of Human Genetics* **22**: 580-6.

²⁹⁵ Joint Committee on Medical Genetics, (2011) *Consent and confidentiality in clinical genetic practice: Guidance on genetic testing and sharing genetic information*, available at: http://www.bsgm.org.uk/media/678746/consent_and_confidentiality_2011.pdf.

“...People quite naturally go for, ‘Okay, what’s the worst case scenario?’ And I think the information that’s presented to them should try to balance that out as much as possible.” (Person with a genetic condition – interviewee)

- 3.21 Genetic counsellors and nurses are widely recognised as integral parts of the multidisciplinary team that provides prenatal diagnosis services.²⁹⁶ A recent report by the All Party Parliamentary Group on Rare, Genetic and Undiagnosed Conditions recommended that the Government should ensure consistent access to genetic counselling services and that the capacity of these services must grow as more people access genetic testing services.²⁹⁷ The Association of Genetic Counsellors and Nurses is currently developing a national workforce planning scheme for genetic counselling services across the UK.²⁹⁸
- 3.22 In addition to the information they receive from NHS healthcare professionals, women and couples who have been referred for prenatal genetic testing or have received a diagnosis are likely to seek information from a variety of other sources, including the NHS Choices website and other websites, as well as patient organisations. This can help women to make informed choices about termination or to prepare for the birth of a disabled child. However, this kind of information also has the potential to create anxiety.

“Yes, Google wasn’t our friend at that time. That made it quite a stressful time, because everything that we came up with was awful, and, yes, we didn’t know what they were testing for, specifically, so we were worried about everything.” (Woman with experience of undergoing NIPT - interviewee)

Given this, it is important that the NHS, as a state institution and well-trusted organisation, ensures women have access to accurate and balanced information, such as through genetic counsellors or through the NHS Choices website. The lack of information on continuation of pregnancy after the diagnosis of a genetic condition on the NHS Choices website is relevant here and should be rectified as soon as possible (see Paragraphs 2.16-2.41 for further discussion on the provision of information and support to women and couples undergoing NIPT).

Prenatal diagnoses

- 3.23 The availability of NIPT for rare genetic conditions in the NHS is still quite limited and is unlikely to have had any impact on the number of prenatal diagnoses yet. It is possible that, in the future, more women with a family history of a genetic condition or with anomalous ultrasound scans may choose to have prenatal diagnostic testing if there is a safe, accurate test available that can be carried out early in pregnancy. Increased uptake may lead to an increase in the number of women receiving positive results, and thus an increase in both the number of women continuing a pregnancy and the number of women terminating a pregnancy. This would have many of the potential implications discussed in Chapter 2 in the context of prenatal diagnoses of Down’s, Edwards’ and Patau’s syndromes (see Paragraphs 2.42-2.63). For example, an increase in the number of women deciding to continue their pregnancy would mean that more women had been able to prepare psychologically and practically for the birth of a baby with a genetic

²⁹⁶ Cordier C, Lambert D, Voelckel M-A, Hosterey-Ugander U and Skirton H (2012) A profile of the genetic counsellor and genetic nurse profession in European countries *Journal of Community Genetics* 3: 19-24.

²⁹⁷ APPG on Rare, Genetic and Undiagnosed Conditions (2016) *Undiagnosed: genetic conditions and the impact of genome sequencing*, available at: <http://www.raredisease.org.uk/media/1860/final-swan-graduate-report.pdf>.

²⁹⁸ Personal communication with the Association of Genetic Counsellors and Nurses.

condition, and enable medical interventions to be offered that could improve the outcomes for the baby.

"I think, knowing what her condition was going to be, or what it was, for sure, I think really helped to plan her care." (Woman with experience of undergoing NIPT - interviewee)

"We had, at least, time to prepare ourselves emotionally but also practically." (Woman with experience of undergoing NIPT - interviewee)

- 3.24 An increase in the number of terminations could be problematic for people who disagree with termination or do not believe that a particular genetic condition, or any condition, is sufficient grounds for termination. If an increase in terminations leads to a significant reduction in the number of people living with a condition, it is plausible that the quality of specialist health and social care received by people with the condition, and the importance attributed to research into the condition will be affected (see Paragraphs 2.50-2.62 for a full discussion of the potential implications of an increase in terminations).

Implications for people with genetic conditions

- 3.25 The 'expressivist objection' to population prenatal screening programmes – that they send a hurtful or disparaging message to disabled people (see Paragraphs 2.65-2.69) – could also be levelled at NHS services that offer prenatal testing for rare genetic conditions. If the increasing availability of NIPT for rare genetic conditions in the NHS increases the number of prenatal diagnoses, it could be seen as reinforcing or amplifying the negative messages sent by existing prenatal testing services about the societal value placed on people with genetic conditions. The availability of NIPT for rare genetic conditions may also upset, distress or offend disabled people and their families, and they might be more vulnerable to discrimination, stigma or abuse if people come to perceive that parents are 'to blame' for having a baby with a disability because of choices they made during pregnancy. This may lead to perceptions that it is the family's responsibility to meet the needs of disabled people and no longer any responsibility of the state.

"...My children, should they choose to have children who have an impairment, they will be viewed in a very different way. Because they will have had the choice to not do that." (Person with a genetic condition – interviewee)

"I think if there is less risk to pregnancy, then people maybe will be choosing that [NIPT] more, and faced with a very difficult decision in the context of a society that probably doesn't welcome the idea, really, of lots more disabled people." (Carrier of a genetic condition – interviewee)

- 3.26 Prenatal testing may have benefits for people with genetic conditions by enabling them to make informed choices in pregnancy. People with a genetic condition may have a greater chance of having a child with a genetic condition that they may want to avoid. In some cases their own disability could make it more challenging for them to parent a disabled child themselves.²⁹⁹ Having access to prenatal testing allows people with genetic conditions to exert more control over the circumstances of their pregnancies.

²⁹⁹ Boardman FK (2014) The expressivist objection to prenatal testing: the experiences of families living with genetic disease *Social Science & Medicine* **107**: 18-25.

"[In a] perfect world it will allow for people with genetic conditions to be better prepared..." (Person with a family member or close friend with a genetic condition – survey respondent)

- 3.27 A study of the views of adults with spinal muscular atrophy (SMA) and their families found that 76 per cent were in favour of prenatal screening for SMA. Reasons given included because it would allow families to make informed decisions and it would prevent unnecessary suffering. The downsides of identifying SMA in pregnancy were thought by some to include fewer people with SMA coming into the world who could have lived fulfilling lives, and the loss to society of having fewer people with SMA coming into the world.³⁰⁰ Another study suggested that people with achondroplasia support the availability of genetic testing amongst pregnant women and couples with a higher chance of having an affected pregnancy. Inheriting the homozygous version of the condition, which is usually fatal before or shortly after birth, was seen as something people would benefit from having the opportunity to avoid.³⁰¹ The availability of prenatal testing can, however, lead to conflicting feelings in people with genetic conditions, as articulated by one of the people with a genetic condition who we interviewed during the project:

"Because on one hand I didn't want to negate my life or what I'd achieved, or what I was yet to achieve by saying I wouldn't want to have a disabled child. At the same time, I'm quite aware that it's not an easy life and you wouldn't necessarily wish that on somebody that you loved, or would love." (Person with a genetic condition – interviewee)

Potential future developments

- 3.28 This is a rapidly moving field, and NIPT for other serious single gene conditions, or 'panel tests' for several related conditions, are likely to be developed in future.³⁰² For example, research is exploring ways in which single gene disorders can be detected reliably, using NIPT, even when they are inherited from the mother.³⁰³ It is possible that cells obtained from the cervix may resolve this technical difficulty.³⁰⁴ As discussed throughout this report, the availability of NIPT for significant medical conditions or impairments can enable pregnant women and couples to make informed choices about their pregnancies regarding whether to continue and prepare for the birth of a disabled child, or whether to have a termination.
- 3.29 Some NIPT tests for rare genetic conditions may become candidates for population wide NHS screening programmes in the future. NIPT 'panel tests' for a set of related conditions might be the most likely to be considered for screening programmes, given that the total prevalence of the conditions may be higher than prevalence of individual ones. Any new screening programme must be recommended by the UK National

³⁰⁰ Boardman FK, Young PJ and Griffiths FE (2017) Population screening for spinal muscular atrophy: A mixed methods study of the views of affected families *American Journal of Medical Genetics Part A*: 421-34.

³⁰¹ Gollust SE, Thompson RE, Gooding HC and Biesecker BB (2003) Living with achondroplasia: attitudes toward population screening and correlation with quality of life *Prenatal diagnosis* **23**: 1003-8.

³⁰² See: <http://www.bwnft.nhs.uk/wp-content/uploads/2015/06/NIPT-and-NIPD-NIPSIGEN-articles-to-run-concurrently.pdf>.

³⁰³ Lun FM, Tsui NB, Chan KC *et al.* (2008) Noninvasive prenatal diagnosis of monogenic diseases by digital size selection and relative mutation dosage on DNA in maternal plasma *Proceedings of the National Academy of Sciences of the United States of America* **105**: 19920-5.

³⁰⁴ Jain CV, Kadam L, van Dijk M *et al.* (2016) Fetal genome profiling at 5 weeks of gestation after noninvasive isolation of trophoblast cells from the endocervical canal *Science Translational Medicine* **8**: 363re4.

Screening Committee, based on its criteria for appraising new screening programmes (see Paragraphs 2.92-2.93 for a discussion of the UKNSC's criteria).

- 3.30 As NIPT for more conditions becomes available, women and couples who previously might have considered PGD as a way of avoiding a genetic condition may now have an alternative option that is more attractive than prenatal invasive diagnostic testing. PGD involves undergoing IVF, which can be a stressful and unpleasant process and is often unsuccessful. NIPT allows the couple to conceive naturally, can be carried out at an earlier stage of pregnancy than invasive testing, and is safe and accurate. Those with a positive diagnosis would have to choose a termination to avoid having a child with the genetic condition, and clearly this would be unacceptable to some women and couples.
- 3.31 It may become possible in the future to use NIPT to test for less significant medical conditions and impairments, or for non-medical traits. Sex determination for non-medical reasons using NIPT is already widely available in the private sector (see Paragraphs 4.39-4.48). However, it is unlikely that NIPT for these types of conditions or traits would be made available to NHS patients given that this information has no clinical utility. Any new NIPT test would be subject to evaluation before it was made generally available, and genetics professionals usually would be involved in the offer of prenatal genetic testing to women and couples. These mechanisms are likely to ensure that any test that lacked clinical utility would not be offered to NHS patients and would be deemed to be an inappropriate or disproportionate use of NHS resources. NIPT for adult onset conditions or carrier status, however, may be considered to be services that the NHS ought to offer. We consider the issues raised by offering these kinds of NIPT, if they were to become available in the future, below.

NIPT for adult onset conditions and carrier status

- 3.32 The use of NIPT to test fetuses for genetic conditions that are likely to affect them only in adulthood, if this became available in future, raises a number of issues that require consideration. These issues apply equally to any prenatal testing method, but may be particularly pertinent to NIPT given that the test does not pose any risk to the fetus in the way that current invasive testing does. Even though a fetus does not have the same legal status as a child, it has been suggested that arguments for not testing a child in order to respect the autonomy and protect the privacy and other interests of the future adult also applies to not testing a fetus in a continuing pregnancy.³⁰⁵ This is borne out in clinical practice: if there is no intention to terminate the pregnancy (i.e. when the testing is 'for information only' and the information will not inform medical intervention of any kind), couples are usually advised against prenatal testing for adult onset conditions to enable the future person to decide for themselves if they would like testing.
- 3.33 Considerations that would weigh in favour of allowing prenatal testing for adult onset conditions are the condition being extremely serious, there being no treatment available and termination of pregnancy being an option. Huntington's disease is an example of such a condition. People who have the gene for Huntington's will develop the disease, usually in their 40s or 50s, and there is a 50 per cent chance that any children they have will inherit the gene. Prenatal testing for Huntington's disease is already available within the NHS using invasive testing methods. Sometimes 'exclusion' testing is used, which identifies the chance that the fetus will develop the condition without disclosing whether the parent will be affected. Difficult situations can arise when a couple opts for prenatal testing and it is found that the fetus has the gene for Huntington's disease, but

³⁰⁵ Deans Z, Clarke AJ and Newson AJ (2015) For your interest? The ethical acceptability of using non-invasive prenatal testing to test 'purely for information' *Bioethics* 29: 19-25.

subsequently the couple decides against termination. In these cases, significant information about the health of the future person is known by their parents and medical professionals from birth. In this situation, testing a fetus has removed the future person's ability to make their own choice about accessing this information. Knowing that one is likely to develop a serious, untreatable illness might give rise to significant psychological harms. There is also evidence that many adults who are at risk prefer not to know, and there are no clinical benefits of knowing in the years before children can make that choice for themselves.³⁰⁶ If the information is not disclosed to the future person and 'family secrets' are created, the potential benefits of some types of foreknowledge will be lost (such as those relating to screening for tumours and reproductive choices).³⁰⁷ If it becomes possible to test for Huntington's disease or similar conditions using NIPT and a diagnosis could be provided early in pregnancy, it is possible that there would be fewer cases of couples subsequently deciding against termination. Additional challenges arise due to the ability of invasive prenatal testing to reveal not only whether the fetus has the gene for Huntington's, but also whether a parent has the gene if this is not already known. Careful counselling with genetics professionals is required to enable parents to consider different testing options.

- 3.34 'Carrier testing' is widely offered to women and couples with a known risk of having a gene for a serious condition and who are considering a pregnancy. This applies to conditions that are caused by recessive genes, where people with the condition have inherited the gene for the condition from both parents. Carriers of one gene will not have any symptoms, but their children may inherit the gene. If the person's partner has the condition or is a carrier of the condition, their children may have or develop the condition. Sometimes, carrier status is revealed inadvertently during screening. For example, screening newborn babies for sickle cell disease and cystic fibrosis will identify babies who are healthy carriers of the sickle cell gene variants.
- 3.35 In the future, it may be possible to use NIPT to test whether fetuses are carriers of genetic conditions, or information about carrier status may be revealed even when the primary intention is to test whether the fetus has a genetic condition. Carrier status would not be grounds for termination, and so such information would be 'for information only' and would have no clinical use prenatally. It has been argued that carrier testing of fetuses would normally be inappropriate for the same reasons that apply to prenatal or childhood testing for adult onset conditions, i.e. because it deprives the future person of the opportunity to make their own decision about accessing this information and may give rise to anxiety.³⁰⁸ However, in the case of newborn screening, if a baby is found to be a carrier of sickle cell disease or cystic fibrosis through the newborn screening programme, healthcare professionals are currently advised to report this result to the parents and offer counselling. The result is recorded in the baby's personal child health record and it is recommended that this is communicated to GPs and stored in a secure and accessible format.³⁰⁹ The British Society for Human Genetics agrees that this information should not

³⁰⁶ British Society for Human Genetics (2010) *Report on the genetic testing of children 2010*, available at: http://www.bsgm.org.uk/media/678741/gtoc_booklet_final_new.pdf.

³⁰⁷ We discuss in more detail the range of issues raised when genetic information about future people is accessed prenatally in Chapter 4 (see Paragraphs 4.56-4.59).

³⁰⁸ Deans Z, Clarke AJ and Newson AJ (2015) For your interest? The ethical acceptability of using non-invasive prenatal testing to test 'purely for information' *Bioethics* **29**: 19-25.

³⁰⁹ UK Newborn Screening Programme Centre (2012) *Health professional handbook. a guide to newborn blood spot screening for healthcare professionals*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/390977/Health_Professional_Handbook_2012_v1.0_December_2012.pdf.

be withheld from parents who indicate that they wish to receive it, but suggest that the policy of routine disclosure of carrier test results that carry no medical implications for the child should be re-examined.³¹⁰

NIPT for whole genome or exome sequencing

- 3.36 Whole genome and exome sequencing of fetuses using NIPT has been carried out in a research setting and it is possible that this will be available to NHS genetic testing services in the near future.³¹¹ Whole genome sequencing might be helpful in the diagnosis of a suspected genetic mutation of unknown origin as a kind of 'scatter gun' approach. The UKGTN has already approved a prenatal test that uses whole exome sequencing for couples who have previously lost multiple fetuses in mid or late pregnancy as a result of a suspected but unknown severe genetic disorder (this test is not an NIPT test; it involves amniocentesis). The providers of the test use a data analysis strategy to reduce the likelihood of unexpected findings.³¹²
- 3.37 This kind of testing, however, could produce large amounts of detailed genetic information of uncertain or unknown clinical significance, as well as information about significant medical conditions or impairments, adult onset conditions, carrier status, less significant medical conditions or impairments, and non-medical traits. Potential issues would be raised if this information were communicated to pregnant women and couples. For example, revealing information about the fetus that is of unknown or uncertain clinical significance could undermine the ability of women to make informed reproductive choices and lead more women to have invasive diagnostic procedures. In addition, providing information that is of limited clinical utility may not clearly align with responsibilities of healthcare professionals to ensure patients receive good care and treatment. Although this might be mitigated by the provision of high quality pre- and post-test counselling, the question might be asked as to whether this information should be returned to the pregnant women and couples at all. In addition, if the test revealed information about adult onset conditions, carrier status, less significant medical conditions or impairments or non-medical traits (i.e. those conditions and traits that would generally not be considered grounds for termination), this might be harmful to the future person. If this kind of information were generated and stored, it could undermine the ability of the future person to make their own choices about accessing their genetic information, and may result in the shutting down of some of their future life options (this is discussed in more detail in Paragraphs 4.56-4.57).

"I suppose doing whole-genome sequencing wouldn't seem that alarming in the context of just some parents wanting to know that their baby is going to be born healthy, but that information is still there forever." (Person with a genetic condition – interviewee)

³¹⁰ British Society for Human Genetics (2010) *Report on the genetic testing of children 2010*, available at: http://www.bsgm.org.uk/media/678741/gtoc_booklet_final_new.pdf.

³¹¹ Lo YM, Chan KC, Sun H *et al.* (2010) Maternal plasma DNA sequencing reveals the genome-wide genetic and mutational profile of the fetus *Science Translational Medicine* **2**: 61ra91; Chen S, Ge H, Wang X *et al.* (2013) Haplotype-assisted accurate non-invasive fetal whole genome recovery through maternal plasma sequencing *Genome Medicine* **5**: 18; Chan KC, Jiang P, Sun K *et al.* (2016) Second generation noninvasive fetal genome analysis reveals de novo mutations, single-base parental inheritance, and preferred DNA ends *Proceedings of the National Academy of Science of the United States of America* **113**: E8159-e68.

³¹² UK Genetic Testing Network, (2015) *Gene dossier: lethal fetal/neonatal autosomal recessive disorders whole exome panel*, available at: https://ukgt.nhs.uk/uploads/tx_ukgt/Lethal_Fetal_Neonatal_ARD_GD_Sept_15.pdf; Ellard S, Kivuva E, Turnpenny P *et al.* (2015) An exome sequencing strategy to diagnose lethal autosomal recessive disorders *European Journal of Human Genetics* **23**: 401-4.

- 3.38 If less targeted testing methods are used for women accessing NIPT for rare genetic conditions in future, this might reveal unanticipated or secondary findings, such as clinically relevant genetic information about the pregnant woman, and maternal cancerous or malignant tumours. The EuroGentest guidelines on prenatal diagnostic tests suggest that targeted testing for the condition is preferred where possible to reduce the potential for unanticipated or secondary findings³¹³ but there are calls for more research on patients' experiences to inform best practice for consent and, where relevant, feedback of secondary findings.³¹⁴ In addition, the nature of the test used to identify a rare condition shapes the interpretation of the result, especially if the risk of abnormality is one that family history or an ultrasound scan has raised as a possibility. Targeted tests are less likely to lead to difficulties of interpretation than results generated by whole genome or exome sequencing, especially if neither parent is affected or only the father (i.e. if the suspected condition appears to have been transmitted paternally or to have arisen *de novo*).
- 3.39 Comparable genome-wide results of similar detail are already arising from other methods of prenatal testing, such as chromosomal microarray (CMA) testing (which is carried out on fetal DNA derived using amniocentesis or CVS). The high resolution of CMA testing means that it has an increased rate of diagnosis of chromosome anomaly, but it also detects a large amount of detailed genetic information of uncertain or unknown significance. Research has found that women offered CMA testing in pregnancy had often felt that a wider test would be better, yet the results left them shocked, anxious, confused and overwhelmed. Afterwards, many women considered this information to be knowledge they wished they did not have.³¹⁵ UK professional guidance on the use of CMA in prenatal testing recommends that only findings that inform the management of the pregnancy or of the family should be reported. It is recommended that findings of uncertain significance, or those that have no "clinically actionable consequence" for that child or family in the future, should not be reported.³¹⁶ The American College of Obstetricians and Gynecologists (ACOG) recommends that prenatal CMA testing should only be offered to women undergoing prenatal diagnosis or when a fetal anomaly has been detected on an ultrasound scan. The ACOG suggests that comprehensive pre- and post-test genetic counselling from qualified personnel regarding the benefits, limitations, and results of CMA testing is essential.³¹⁷ The EuroGentest guidelines suggest that targeted testing is preferred where possible to reduce the potential for results with unclear clinical significance.³¹⁸

³¹³ Skirton H, Goldsmith L, Jackson L, Lewis C and Chitty L (2014) Offering prenatal diagnostic tests: European guidelines for clinical practice *European Journal of Human Genetics* **22**: 580-6.

³¹⁴ Dheensa S, Shkedi-Rafid S, Crawford G *et al.* (2016) Management of incidental findings in clinical genomic sequencing studies, in *eLS* (Wiley Online Library).

³¹⁵ Bernhardt BA, Soucier D, Hanson K *et al.* (2012) Women's experiences receiving abnormal prenatal chromosomal microarray testing results *Genetics in Medicine* **15**: 139-45.

³¹⁶ Joint Committee on Genomics in Medicine (2015) *Recommendations for the use of chromosome microarray in pregnancy* available at: http://www.bsgm.org.uk/media/956141/g144_useofcmapregnancy_jun15.pdf.

³¹⁷ Gregg AR, Skotko BG, Benkendorf JL *et al.* (2016) Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics *Genetics in Medicine* **18**: 1056-65, American College of Obstetricians and Gynecologists and Society for Maternal-Fetal Medicine (2013) *The Use of Chromosomal Microarray Analysis in Prenatal Diagnosis*, available at: <https://www.acog.org/-/media/Committee-Opinions/Committee-on-Genetics/co581.pdf?dmc=1&ts=20161118T1012543014>.

³¹⁸ Skirton H, Goldsmith L, Jackson L, Lewis C and Chitty L (2014) Offering prenatal diagnostic tests: European guidelines for clinical practice *European Journal of Human Genetics* **22**: 580-6.

Chapter 4

NIPT in the private sector

Chapter 4 – NIPT in the private sector

Chapter overview

Non-invasive prenatal testing (NIPT) is available on a private basis to women and couples through hospitals and clinics in the UK. All of the NIPT tests on the market estimate the chance that a fetus has Down's, Edwards' and Patau's syndromes. Some also test for sex and genetic variations such as sex aneuploidy and microdeletions. For the majority of women, privately-sought NIPT offers reassurance at an early stage of pregnancy.

Many NIPT tests being carried out by UK hospitals and clinics are sent to the USA or China for analysis, and so fall outside UK and EU laws that regulate medical devices. However, the healthcare professionals offering NIPT in the UK are obliged by their regulating bodies to ensure patients have given properly informed consent to care or treatment. In addition, providers must ensure their advertising material is not misleading or harmful.

Although there are some examples of good practice, there is commonly a lack of good quality information from manufacturers, private hospitals and clinics about the limitations of NIPT and the conditions being tested for. The availability of impartial information and support from independent organisations and the NHS is important.

There are concerns that the support offered by private NIPT providers to women with a high chance NIPT result can be inadequate, particularly in direct-to-consumer contexts. Women with these results seek follow-up advice and support, invasive diagnostic testing and termination services in the NHS.

There is scant or unreliable information on the accuracy of NIPT when used to test fetuses for sex aneuploidy and microdeletions. Where test performance data are available, false positive rates are often much higher, which could lead to more women seeking unnecessary invasive diagnostic tests and increased anxiety.

The offer of NIPT to find out the sex of the fetus at an early stage in pregnancy may increase the risk of sex selective terminations taking place. This practice is opposed by many, believing it to be sexist and wrong. There is some evidence that sex selective terminations have happened in the UK, and they are known to occur in other countries. It is also known that people who live in countries where prenatal sex determination is illegal travel to countries where it is legal to have such tests.

As manufacturers compete with each other for their share of market, it is plausible that the trend of offering NIPT for more conditions and traits will continue. Allowing women and couples to access NIPT for less significant medical conditions or non-medical traits would have limited clinical utility, may lead to selective terminations, and may threaten the autonomy and interests of the future person.

The same concerns are raised by the prospect of NIPT for whole genome or exome sequencing of fetuses becoming available in the private sector. In addition, much of the information generated would be difficult to interpret, potentially causing unnecessary anxiety to pregnant women and couples.

Introduction

- 4.1 Pregnant women and couples in the UK have been able to access non-invasive prenatal testing (NIPT) for Down's syndrome in the private sector since 2012. There are a number of different test brands on the market including the Harmony™ test offered by Ariosa Diagnostics (Roche; USA), the MaterniT21™ test offered by Sequenom (USA), the Panorama® test offered by Natera (USA), the Nifty™ test offered by BGI Genomics (China), the Verifi® test offered by Illumina (USA), the Iona™ test offered by Premaitha Health (UK) and Serenity™ test offered by Genesis Genomics (UK). NIPT is offered in over 60 countries³¹⁹ and the global NIPT market is forecast to grow at an annual rate of 17 per cent between 2016 and 2020.³²⁰

Current availability and regulation

- 4.2 Most test manufacturers only offer NIPT to women on a private basis through hospitals and healthcare clinics, although some clinics are located in retail outlet chains on high streets. A woman wanting the test will need to attend a clinic and go through a process of consultation and consent before a blood sample is taken and sent for analysis. Most hospitals and clinics send the blood sample to the test manufacturer for analysis, although some have in-house analysis facilities. Women typically wait for between one and two weeks to receive their results. NIPT is also available to women in the UK on what might be considered a direct-to-consumer basis from a small number of test suppliers. A test kit can be ordered directly from the suppliers' websites, which is sent to the woman's doctor, who then takes a blood sample to be sent for analysis. With this service, results are delivered within five working days.
- 4.3 The tests can be carried out from nine or ten weeks of pregnancy and cost around £400-£600, depending on whether other tests are included, such as a viability scan. All of the tests on the market assess the chance that the fetus has Down's, Edwards' and Patau's syndromes. Some test manufacturers also offer to test for sex and genetic variations such as sex aneuploidy and conditions caused by microdeletions (see Paragraphs 1.28-1.29). NIPT for single gene disorders, such as cystic fibrosis and skeletal dysplasias, is also available through private hospitals in the same way that this is available through the NHS to women and couples with a family history of a genetic condition or if anomalies are seen on an ultrasound scan. This is a paid-for service provided by local genetics testing services rather than by one of the commercial suppliers of NIPT.
- 4.4 The manufacture and sale of NIPT tests in the UK are regulated by the UK Medical Devices Regulations 2002,³²¹ which implement the EU In-Vitro Diagnostic Medical Devices (IVD) Directive. The aim of the EU Directive is to ensure that medical devices are safe and of high quality. Unlike medicines, medical devices are not subject to pre-market authorisation, but manufacturers must ensure that the device meets certain 'essential requirements'. The Directive aims to ensure that the devices do not compromise the health and safety of patients and users, and that they achieve the performance specified by the manufacturer for the stated medical purpose. NIPT tests fall into the moderate-risk category, which requires the involvement of a notified body to

³¹⁹ Allyse M, Minear MA, Berson E *et al.* (2015) Non-invasive prenatal testing: a review of international implementation and challenges *International Journal of Women's Health* 7: 113-26.

³²⁰ Research and Markets (2016) *Global non-invasive prenatal testing market 2016-2020*, available at: <http://www.researchandmarkets.com/research/vt4hv2/global>.

³²¹ Part IV of The Medical Devices Regulations 2002, available at <http://www.legislation.gov.uk/uksi/2002/618/part/IV/made>.

evaluate whether the device complies with the Directive. In the UK, the Medicines and Healthcare Products Regulatory Agency (MHRA) is the competent authority for the Directive and it designates notified bodies to carry out assessments of devices. Manufacturers are also required to operate a post-market surveillance system. If risk of serious injury or death has been noted, the manufacturer is required to report this to the MHRA. Devices that adhere to the Directive can apply for a CE mark and then be sold anywhere in the EU. Manufacturers must have evidence to support the claims they make, and devices must meet the claims made for them, but there are no minimum performance specifications set out in the Directive.

- 4.5 The Directive will soon be replaced by the EU IVD Regulation, which will come into force in 2017 with a five-year transition period. EU regulations apply directly in all EU countries and do not require transposition into national law. Under the new Regulation, IVD manufacturers are likely to be required to produce significantly more evidence on clinical performance, including diagnostic sensitivity, diagnostic specificity, positive predictive value and negative predictive value. The most recent draft of the Regulation states: "Devices shall be designed and manufactured in such a way that they are...suitable with regard to the performance taking account of the generally acknowledged state of the art."³²² It has been suggested that this would be a step towards manufacturers becoming fully responsible for the clinical utility of their devices.³²³
- 4.6 The EU Directive/Regulation does not regulate testing services, only the devices used in the testing services when they are placed on the market in the EU. Therefore, if a blood sample is taken in an EU country but sent outside of the EU for analysis, this device is not covered by the EU Directive/Regulation. Currently, many NIPT tests being carried out by UK hospitals are sent to the USA or China for analysis, and so fall outside the EU Directive/Regulation. The UK's decision to leave the EU also throws into question the future relevance of the EU Directive/Regulation to NIPT services being carried out in the UK.
- 4.7 All US manufacturers of NIPT kits market their tests as laboratory-developed tests (LDTs) and the US Food and Drug Administration (FDA) has so far decided not to regulate LDTs. However, in 2012, the FDA suggested that it was considering extending its oversight to NIPT and some US manufacturers have indicated they have plans to seek premarket approval from the FDA for NIPT kits in the future. There is no clear consensus in the USA about whether NIPT kits should be regulated by the FDA.³²⁴ In China, the regulation of *in vitro* medical devices was strengthened in 2014. NIPT kits belong to the highest risk category, and require registration by the China Food and Drug Administration. One hundred and eight hospitals have been approved to provide NIPT kits for Down's, Edwards' and Patau's syndromes, but the detection of fetal sex is prohibited for pregnant women in China.³²⁵
- 4.8 This regulation, or lack of regulation, of NIPT applies equally to the NIPT that is on offer in the NHS as it does to its provision in the private sector. In fact, NIPT in the NHS might be considered to be even less regulated, given that genetic tests that are manufactured

³²² Proposal for a Regulation of the European Parliament and of the Council on *in vitro* diagnostic medical devices, available at: <https://www.emergogroup.com/sites/default/files/europe-ivd-regulation-consolidated-negotiated-text.pdf>.

³²³ BSI (2016) *How to prepare for and implement the upcoming IVDR – Dos and don'ts.*, available at: [http://www.bsigroup.com/LocalFiles/EN-AU/ISO%2013485%20Medical%20Devices/WP12_How_to_prepare_for_and_implement_the_upcoming_IVDR___Dos_and_Don___ts%20\(1\).pdf](http://www.bsigroup.com/LocalFiles/EN-AU/ISO%2013485%20Medical%20Devices/WP12_How_to_prepare_for_and_implement_the_upcoming_IVDR___Dos_and_Don___ts%20(1).pdf).

³²⁴ Allyse M, Minear MA, Berson E *et al.* (2015) Non-invasive prenatal testing: a review of international implementation and challenges *International Journal of Women's Health* 7: 113-26.

³²⁵ Zeng X, Zannoni L, Löwy I and Camporesi S (2016) Localizing NIPT: Practices and meanings of non-invasive prenatal testing in China, Italy, Brazil and the UK *Ethics, Medicine and Public Health* 2: 392-401.

and used in-house by health institutions, such as NHS hospitals, are exempt from many parts of the Directive. However, there are a number of important differences between the use of NIPT in the NHS and the use of NIPT in the private sector. Any NIPT tests that might be considered for an NHS population screening programme must be approved by the UK National Screening Committee against its assessment criteria, as happened recently with proposals for NIPT to be used to test for Down's, Edwards' and Patau's syndromes. It is the responsibility of Public Health England to ensure screening programmes are delivered with the appropriate information and support. When NIPT is offered to women who have a family history of a genetic condition, it is usually offered with the support of NHS genetic counsellors to help women interpret their results and consider their options. The UK Genetic Testing Network evaluates the scientific validity and clinical utility of new genetic tests that its member laboratories would like to offer NHS patients. The offer of NIPT in the private sector, on the other hand, is subject to no assessment processes and there are no specific obligations on private manufacturers, hospitals and clinics to provide information and support.

- 4.9 However, the healthcare professionals that offer and provide NIPT services in the private sector must adhere to the standards set by their professional regulators such as the General Medical Council (GMC) and the Nursing and Midwifery Council (NMC). Many are also members of one of the Royal Colleges, such as the Royal College of Obstetricians and Gynaecologists and the Royal College of Midwives, which provide continuing professional development for their members and develop guidance for clinical practice. In addition, all providers of 'regulated activities', which includes diagnostic and screening procedures, are regulated by the Care Quality Commission (CQC) in England, and they must carry out these activities to fundamental standards of quality and safety. However, NIPT is only within scope of the CQC's responsibilities when the test is carried out as part of the planning or delivery of an individual's treatment or care, or as part of an NHS screening programme, rather than on a one-off basis. Equivalent bodies in Scotland, Wales and Northern Ireland regulate the quality of care provided by hospitals and clinics in their respective countries (see Paragraph 1.43).
- 4.10 Any advertising of products and services, including NIPT, is monitored by the Committee of Advertising Practice (CAP), which produces codes of conduct for advertising in broadcast and non-broadcast media. The codes stipulate that advertisements must not be misleading, harmful or offensive. The rules in the codes are enforced by the Advertising Standards Authority (ASA). Following a complaint, the ASA can direct advertisers to change their advertising material. If the advertiser does not comply, the case is referred to Trading Standards, which can prosecute the advertiser in the criminal court or apply other kinds of sanctions, such as issuing fines or court orders. The Nuffield Council on Bioethics previously recommended that responsible authorities pay more attention to whether genetic test providers are making clinical claims for their products, even if implied rather than explicit.³²⁶ However, the ASA has not had cause to investigate any NIPT advertisements to date.³²⁷

³²⁶ Nuffield Council on Bioethics (2010) *Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age*, available at: <http://nuffieldbioethics.org/personalised-healthcare>.

³²⁷ Personal communication with the Advertising Standards Authority.

Implications of NIPT in the private sector

Test safety and performance

- 4.11 Evidence shows that NIPT is a safe and accurate test for predicting Down's, Edwards' and Patau's syndromes in fetuses. It is possible that the availability of NIPT in the private sector for these conditions is reducing the number of women currently having invasive diagnostic testing after a high chance result from the NHS combined test. If such women have already received a low chance result from privately accessed NIPT (which is highly likely to be accurate), this would suggest that the combined test result is false, and so no further testing is necessary. However, women will be able to access this information in the NHS from 2018, when NIPT for Down's, Edwards' and Patau's syndromes is introduced as a second stage test in the fetal anomaly screening programme.
- 4.12 NIPT for Down's, Edwards' and Patau's syndromes is less accurate in pregnant women who access it as a first stage test than in women having NIPT as a second stage test following a high chance combined test result (see Box 1.3, p13). This is because the accuracy of NIPT for Down's, Edwards' and Patau's syndromes involves population statistics that vary depending on the prevalence of the conditions in the population. Prevalence is lower in the general population compared to the population of women with a high chance result following combined testing. However, even when NIPT is carried out on pregnant women as a first stage test, NIPT is more accurate than the combined test (see Box 1.2, p8).
- 4.13 The offer by some NIPT manufacturers to test for other genetic variations, such as sex aneuploidy and microdeletions, was a cause for concern for many of the individuals and organisations we consulted during the project for a number of reasons. The use of NIPT for these variations has not been widely researched, meaning that there is little or unreliable information available on test accuracy for potential customers.³²⁸ Where information about test performance is available, often the accuracy of NIPT for these other variations is much lower than the accuracy of NIPT for Down's, Edwards' and Patau's syndromes and, in particular, the chance that a result is false is much higher. Women who receive a high chance result are likely to be very anxious about this. We heard anecdotal evidence that NHS staff are helping women interpret results of this kind and, more seriously, that they can lead to women seeking diagnostic procedures, either in the NHS or in the private sector.

"A particularly unwelcome possible implication is that more invasive tests are actually carried out than currently if women choose to have testing for a wider range of conditions including microdeletions and microduplications and so the screen positive rate increases." (Jane Fisher, Director, Antenatal Results and Choices (ARC) – consultation respondent)

- 4.14 Similarly to women accessing NIPT in the NHS, there is the possibility of unanticipated or secondary findings for women accessing NIPT in the private sector, such as clinically relevant genetic information about the pregnant woman and cancerous and malignant maternal tumours. The possibility of these kinds of findings occurring exists only with some kinds of laboratory and processing methods. The NIPT test providers that we spoke to have different policies on reporting unanticipated or secondary findings. Some

³²⁸ Lo KK, Karampetsou E, Boustred C *et al.* (2016) Limited clinical utility of non-invasive prenatal testing for subchromosomal abnormalities *American Journal of Human Genetics* **98**: 34-44.

use technology that masks any findings other than those requested by the pregnant woman. Others usually inform the woman's doctor about any such findings and allow the doctor to make a judgment about whether to inform the woman.³²⁹ The American College of Medical Genetics and Genomics (ACMG) recommends informing women of the possibility of identifying maternal genomic anomalies and that this possibility depends on the specific methodology used, and that women should be referred to a trained genetics professional when NIPT identifies maternal genomic anomalies.³³⁰ There are calls for more research on patients' experiences to inform best practice for consent and, where relevant, feedback of secondary findings.³³¹

- 4.15 As discussed earlier, there is the possibility of test failure and inconclusive or indeterminate results with NIPT. As with women accessing NIPT through the NHS, it will be important that women and couples are aware of the possibility of failed or inconclusive tests before consenting to NIPT.
- 4.16 It should be noted that most of the research that has been carried out on the performance of NIPT in different populations has been funded by manufacturers of NIPT. In a review of studies on NIPT, the risk of bias due to the role of the sponsor was suggested to be high in most of the studies that were considered.³³² Research in this area is likely to continue to be driven and funded by the private sector, and any evidence that derives from this research should be treated with appropriate caution.

Access

- 4.17 Women who access NIPT through a private hospital or clinic can have the test at an early stage of pregnancy from nine or ten weeks, and will receive the results within one to two weeks. Those with a low chance result will receive reassurance at an early stage, earlier than if they had screening through the NHS, reducing anxiety they may have had about their fetus having a genetic condition. Women with a high chance result from private NIPT and who want a confirmed diagnosis will be offered chorionic villus sampling (CVS), which can be carried out from eleven weeks of pregnancy. This means that some women could get a diagnosis earlier than if they had gone through the NHS screening route. Currently, NIPT in the private sector is also being accessed by women who have been identified as having a high chance of their fetuses having Down's, Edwards' or Patau's syndromes following the combined test at 10-14 weeks of pregnancy, and who wish to have NIPT before deciding whether to have invasive diagnostic testing. From 2018, these women will be offered NIPT in the NHS.
- 4.18 Only women and couples with the financial means can access NIPT through the private sector. When NIPT is introduced in the NHS, only women receiving a high chance result from the NHS combined test will be able to access NIPT at no cost, and this will be several weeks later than it can be accessed privately. Some may view this unequal access as unfair. However, NIPT is not unique in being a healthcare service that only some people can access through the private sector. Given that the NHS is not currently

³²⁹ Personal communication with NIPT manufacturers.

³³⁰ Gregg AR, Skotko BG, Benkendorf JL *et al.* (2016) Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics *Genetics in Medicine* **18**: 1056-65.

³³¹ Dheensa S, Shkedi-Rafid S, Crawford G *et al.* (2016) Management of incidental findings in clinical genomic sequencing studies, in *eLS* (Wiley Online Library).

³³² Taylor-Phillips S, Freeman K, Geppert J *et al.* (2016) Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis *BMJ Open* **6**: e010002.

planning to offer NIPT to all pregnant women, others might view the fact that women who are not eligible for free NIPT in the NHS can access NIPT through the private sector as improving access to healthcare. In addition, there are reasons other than financial for not offering NIPT as a first stage test to all pregnant women in the NHS (see Paragraphs 2.13-2.14).

- 4.19 There are several intellectual property disputes between NIPT manufacturers that are currently ongoing.³³³ It is unknown when these disputes will be resolved or what their likely outcomes will be. However, if one NIPT manufacturer successfully wins the sole rights to intellectual property that is vital to other manufacturers' services, the choice available to women seeking NIPT in the private sector may be curtailed and prices may be affected.
- 4.20 There are a number of possible effects on the private sector of NIPT becoming available in the NHS as a second stage screening test. It could increase sales, by raising awareness of the existence of NIPT generally, leading women to seek it as a first stage test early in pregnancy. Women who are just outside the cut-off point for qualifying for NIPT following the combined test might also be motivated to seek the test privately. On the other hand, women who might previously have paid for the test may wait and access it in the NHS if they receive a high-chance combined test result.

Marketing and the provision of information and support

- 4.21 NIPT manufacturers and private hospitals and clinics advertise and provide information about their services directly to pregnant women and couples through websites, patient leaflets and consent forms. Research suggests that although there are some examples of the provision of balanced and accurate information, there is a widespread lack of high quality information provided by manufacturers and private hospitals and clinics on their websites and in their patient leaflets. Information has been found to be frequently incomplete, unsubstantiated, inaccurate or misleading. In addition, the language used can be emotive.³³⁴ This has the potential to cause harm by creating confusion and anxiety among women and couples seeking NIPT services in the private sector and to affect their ability to make informed choices.
- 4.22 Our own review of information made available on the websites and in patient leaflets of manufacturers, hospitals and clinics provided a similar impression. For example, we found that some providers were very clear about the need to follow an NIPT result with invasive testing in order to get a confirmed diagnosis. Other providers described NIPT as "detecting fetal chromosomal abnormalities" or able "to determine whether a pregnancy has certain chromosomal conditions," which does not, in our view, clearly communicate that NIPT is not diagnostic. The accuracy of NIPT was emphasised by the majority of providers we looked at, with it usually being described as "99 per cent accurate." It was not always made clear that the accuracy differs for the different conditions tested for, and the chance that the result could be false was not routinely mentioned and rarely explained. If it was there, detailed information about accuracy (i.e. specificity, sensitivity, positive predictive value and negative predictive value) was often hard to find. There was variation in how clearly providers described the process of undergoing NIPT, including how and when women would receive their results. Most

³³³ Premaita Health plc (2016) *Progress on anti-trust objections to litigation*, available at: www.premaita.com/news/press-releases/20-news/481-4-july-2016-progress-on-anti-trust-objections-to-litigation.

³³⁴ Skirton H, Goldsmith L, Jackson L, Lewis C and Chitty LS (2015) Non-invasive prenatal testing for aneuploidy: a systematic review of Internet advertising to potential users by commercial companies and private health providers *Prenatal diagnosis* **35**: 1167-75.

providers focused on the speed of results, stating how many days or weeks it will take to receive results after the test. Advice to consider seeking genetic counselling following a high chance result was given only by some manufacturers. Those that did mention this emphasised its importance, and some offered the services of their own genetic counsellors. Explanations of the conditions being tested for tended to describe the conditions in terms of their genetics and the associated physical and cognitive disabilities. Explanations tended to be brief, with only some providers including links to sources of further information. We found only one manufacturer that mentioned the possibility of unanticipated or secondary health findings about the mother.

- 4.23 Overall, the information available tended to focus on the potential for the test to provide reassurance, without adequately preparing the woman and couple for the possibility of a high chance (but not diagnostic) result, a false result or a test failure. The names of many of the test brands also might be thought to imply that reassurance would be provided. Even using the term ‘non-invasive’ might give an overly positive impression of the test. Respondents to the survey and consultation had similar views.

“Information provided by clinics on line is more about advertising and promoting the product than promoting informed choice.” (Jane Fisher, Director, Antenatal Results and Choices (ARC) – consultation respondent)

“The website of [private clinic] which offers NIPT presents it very much as offering reassurance to parents, rather than as something which can itself create serious anxiety and very serious ethical problems.” (Anscombe Bioethics Centre – consultation respondent)

- 4.24 This is not the only kind of information that women receive: further information and support are provided by healthcare professionals involved in the delivery of private NIPT at hospitals and clinics. We heard varying reports from respondents to our survey and consultation of the levels of quality of the information and support that are provided. Some felt that the information and support they had received were good, while others felt that they had been misled or were unsupported in some ways.

“Excellent private care given. Most importantly, they had time for us and we felt like they cared.” (Person with experience of undergoing NIPT – survey respondent)

“The doctor performing the test was very good, although she misled us by saying that the NIPT was diagnostic and virtually 100% reliable.” (Person with multiple interests in NIPT – survey respondent³³⁵)

“Some private services give very good information and follow-up. Other services can give very poor follow-up if the result requires further investigation and send women back to the NHS without any communication.” (Healthcare professional – survey respondent)

- 4.25 Several respondents criticised the reflex test, where a blood sample taken from pregnant women at the time of the combined test is automatically used for NIPT on women who are found to have at least a 1 in 800 chance of having a fetus with Down’s, Edwards’ or Patau’s syndromes. This involves women consenting to a test that may or may not be

³³⁵ Survey respondent with experience of undergoing NIPT and a family member or close friend with a genetic condition.

carried out. The providers of this service highlight that this approach “avoids the need to recall women for a second blood test and so avoids causing unnecessary anxiety”.³³⁶ However, some respondents were concerned that this process may not provide women with adequate opportunity for discussion and reflection, and could compromise their ability to give informed consent to NIPT.

- 4.26 We heard a range of examples of how women had received their results. Good practice examples of result-giving that came to our attention include one in which a doctor arranged, before the test was carried out, a specific time to call a couple when they would both be at home in order to deliver their NIPT results. However, we heard of several cases where women were given high chance NIPT results or a diagnosis at inappropriate times or in an inappropriate manner. We also saw examples of results letters that appeared to confuse the accuracy of NIPT in the general population with the likelihood that the woman in question had an affected pregnancy, directed the woman towards amniocentesis, and took an unduly business-like tone. Some NIPT manufacturers have genetic counsellors available to talk to women who have received a high chance result. However, a lack of follow-up support following a high chance result and a reliance on the NHS to ‘pick up the pieces’ was an area of concern for some.

“My results were delivered via a telephone call on a Friday teatime. I was then told if I needed to know more to phone back on Monday in the meantime arrangements would be made to facilitate a termination.” (Person with a family member or close friend with a genetic condition – survey respondent)

“Anecdotal evidence suggests that women are seeking confirmatory invasive testing in the NHS, and in some instances express concern and anxiety regarding the meaning of results from private providers.” (PHG Foundation – consultation respondent)

- 4.27 The information and support that are provided to women undergoing NIPT for the additional genetic variations that some NIPT manufacturers offer to test for, such as sex aneuploidy and microdeletions, were areas of particular concern. Some of these conditions have either highly uncertain prognoses or might not be generally considered to be significant medical conditions or impairments. Triple X syndrome, for example, in which girls have an additional X chromosome, is associated with normal physical development and fertility, and occasionally delayed learning, decreased muscle tone and kidney problems. Van der Woude syndrome, which is caused by a microdeletion, is associated with a cleft lip and palate, but otherwise development can be normal (depending on the exact genetic cause). Anecdotally, we heard that NHS staff are spending significant amounts of time helping women consider their results and options following private tests for conditions such as these. Support of this kind is not available to or accessed by all women, and the fact that NIPT manufacturers offer to test prenatally for these conditions may send the message that they are serious, which may affect women’s choices about termination.

- 4.28 In summary, the information and support provided by the private sector may in some cases be affecting the ability of women and couples to make informed choices about NIPT. They also have the potential to cause harm, such as increased shock, distress and confusion on the receipt of a high chance result, or even the termination of an unaffected fetus if the chance of a false positive result is not clearly communicated. In

³³⁶ Wolfson Institute of Preventative Medicine, Queen Mary University of London (2017) *In-house Antenatal reflex DNA screening for Down’s syndrome, trisomy 18 and trisomy 13*, see: <http://www.wolfson.qmul.ac.uk/newsandevents/in-house-antenatal-reflex-dna-screening-for-down-s-syndrome-trisomy-18-and-trisomy-13>.

the Working Group's view, the information and support provided to women seeking NIPT should be of the same high standard whether they are provided in the NHS or the private sector. Although women and couples accessing NIPT in the private sector will have actively sought out NIPT services rather than being offered them as part of NHS care, the information that they need in order to make informed choices and avoid harm is the same.

- 4.29 Therefore, the websites of NIPT manufacturers and private hospitals and clinics should provide accurate, balanced and accessible information on the performance of NIPT for different conditions and in different women, including its specificity, sensitivity, positive predictive value and negative predictive value. Worked examples of what different test results mean for different women may be helpful; for example, if a high chance test result has been received, how confident can the woman be that the result is accurate. It should be clear that NIPT is not diagnostic and that an invasive test is required to confirm a high chance result. The fact that difficult choices may need to be made as a result of having NIPT should be raised. Up-to-date, balanced and non-directive information should be provided about the conditions being tested for, or at least links to sources of information of this sort should be provided. Providers should consider guidance produced in 2010 by the Human Genetics Commission on the information that should be provided to potential consumers by companies offering genetic testing.³³⁷ Putting a recognised mark of quality on information that meets these standards could enable women and couples to know that such information has been checked and can be trusted. For example, NHS England runs a certification scheme called the Health Information Standard, which enables organisations to add its quality mark logo following an assessment of the information that they provide. It stipulates that information must be clear, accurate, evidence-based, up-to-date and easy to use. Currently, few private health companies are members of this scheme.³³⁸
- 4.30 In addition, healthcare professionals involved in offering and providing NIPT services should understand the accuracy of NIPT in different women and for different conditions, and they should understand the risks associated with diagnostic testing. They should be knowledgeable about what it is like to have a son or daughter with Down's syndrome and how this can vary substantially. There will need to be a sufficient amount of time to discuss NIPT and the conditions being tested for with women before the test. Women who receive a high chance result should be informed in an appropriate way and be given non-directive information about the implications of the result, the condition that has been detected, and the options available. Women should be given opportunity to discuss the results with a skilled healthcare professional soon after they receive them.

Direct-to-consumer NIPT

- 4.31 We are aware of some companies that allow pregnant women to order NIPT for Down's, Edwards' and Patau's syndromes directly through their websites, without requiring them to go through a hospital or clinic, for a cost of approximately £400. The information provided on these websites about NIPT and the conditions being tested for is sparse. Although it is stated that the test must be performed under the guidance of an

³³⁷ Human Genetics Commission (2010) *A common framework of principles for direct-to-consumer genetic testing services*, available at: <https://www.cellmark.co.uk/pdfs/HGCprinciples.pdf>.

³³⁸ See <https://www.england.nhs.uk/tis>.

obstetrician, gynaecologist or related specialist, the kit is sent to a place of the customer's choosing.

- 4.32 Some respondents to our consultation and survey suggested that there could be benefits of NIPT being available on a direct-to-consumer basis. For example, this kind of service could improve access to NIPT among women who live long distances from a clinic, who have mobility issues or who fear stigmatisation from having NIPT at a clinic. It may also be cheaper and quicker to access NIPT in this way. However, others were concerned that, without ready access to a healthcare professional, direct-to-consumer NIPT might increase the risk of the limitations and implications of NIPT not being fully understood, high chance results being misinterpreted, and women feeling unsupported. It may also increase the risk of women seeking a termination on the basis of a NIPT result alone.

"The face-to-face consultation can allow clinicians to offer their patients a clearer picture of how NIPT could affect them based on past experiences with other patients. Buying a test independently, especially if these tests were marketed in convincing or misleading ways, could leave pregnant women very unprepared for an unexpected test result." (Rachel Siden – consultation respondent)

- 4.33 In the Human Genetics Commission 2010 report on direct-to-consumer genetic testing services, tests that provide genetic information about a fetus are highlighted as potentially having a high impact on the consumer, and providers are asked to consider whether these kinds of test results should be provided only in the context of a consultation with a suitably qualified health professional.³³⁹

Other sources of information and support

- 4.34 Women and couples are also likely to access information about private NIPT from a range of other sources, such as online forums, social media and organisations offering advice on prenatal screening. The Antenatal Results and Choices (ARC) website provides information about private providers of NIPT and a checklist of questions for women to ask private providers before making a decision about having the test. Through its helpline, ARC also regularly speaks to women who have received a positive NIPT result through a private provider, offering support and advice on their options. Impartial information and support from an independent organisation such as ARC is important for women and couples who are considering having NIPT in the private sector. As noted previously, however, some may consider that receiving funding from NIPT manufacturers challenges ARC's claims of impartiality.

Implications for the NHS

- 4.35 The availability of NIPT in the private sector already appears to be having an impact on NHS staff and services. We heard that women with high chance NIPT results are seeking advice and support, invasive diagnostic testing and termination services in the NHS. Women who have received conflicting results from privately-sought NIPT and the NHS combined screening test may need particular help in considering their options. How the NHS will meet demand for this kind of support and services was a source of concern for some respondents to our consultation.
- 4.36 Earlier we discussed the important role that organisations that are independent of the private sector could play in providing impartial, accurate and balanced information on

³³⁹ Human Genetics Commission (2010) *A common framework of principles for direct-to-consumer genetic testing services*, available at: <https://www.cellmark.co.uk/pdfs/HGCprinciples.pdf>.

NIPT (Paragraph 4.34). The NHS is a highly trusted organisation and is likely to be sought out by pregnant women who need information and advice in relation to private NIPT. NHS midwives are likely to be the first port of call for women seeking in-person advice. Currently, many NHS midwives are likely to be ill-equipped to provide adequate information and support to women considering NIPT or who have high chance NIPT results, given that NIPT is not yet widely available in the NHS. This may change if healthcare professional training on NIPT is more widely provided with the introduction of NIPT in the NHS. However, midwives are still likely to lack knowledge on NIPT for the other conditions that private NIPT manufacturers offer to test for. The potential increase in workload for NHS midwives and other NHS staff involved in caring for women following a high chance NIPT result was a source of concern for consultation respondents.

“Other concern is the opportunity for private clinics to test for genetic mutations without a clinical genetic support network to discuss results in an informed way. I can just imagine women turning up to a random DGH [District General Hospital] antenatal clinic with a complicated genetics result and there being no system in place as to how to provide reliable information.” (British Maternal and Fetal Medicine Society – consultation respondent)

“This will lead to a greater unwieldy burden upon the NHS. There is a lack of skills, time and scientific knowledge to interpret the reports as they include more and more detail.” (Down Syndrome Research Foundation UK – consultation respondent)

- 4.37 Information provided online by the NHS or other Government funded organisations could also play an important role in providing independent information and advice. The UK National Screening Committee (UKNSC) has produced a booklet for people seeking screening tests in the private sector more generally.³⁴⁰ However, the NHS Choices website, which is one of the primary sources of health information in the UK, does not include information about treatments or tests that are available only in the private sector.
- 4.38 In Chapter 2, we discussed concerns about how the offer of NIPT in the NHS might reduce demand for invasive diagnostic procedures, which could lead to a loss of skills and reduced access to services (see Paragraph 2.81). However, increased use of NIPT in the private sector, particularly for conditions that have high rates of false results, conversely may lead to an increase in demand for invasive diagnostic testing services in the NHS. Given that one of the main benefits of NIPT is purported to be a reduction in the number of women having invasive procedures, this would be highly undesirable. Alongside the potential for any increase in demand to affect numbers of procedure-related miscarriages, it may also create further demands on NHS resources. Some respondents to the consultation were of the view that it is the responsibility of private hospitals and clinics to provide the necessary support and diagnostic testing services following high chance NIPT results. Some private hospitals and clinics do already provide this, and sometimes it is included as part of the NIPT package.

“We believe it is incumbent upon private providers to take responsibility for the whole pathway and be in a position to offer quality assured diagnostic services when

³⁴⁰ UK National Screening Committee (2014) *Thinking of having a private screening test?*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/393609/Public_leaflet_-_Thinking_of_having_a_private_screening_test_FINAL_Nov_2014.pdf.

necessary.” (Jane Fisher, Director, Antenatal Results and Choices (ARC) – consultation respondent)

Sex determination

- 4.39 If they wish, most women and couples are able to find out the sex of the fetus at the NHS 18-20 week ultrasound scan. Now, women and couples accessing NIPT in the private sector can find out the sex of the fetus from nine or ten weeks of pregnancy. Most manufacturers of NIPT offer to test for sex, which can be selected by women when accessing NIPT through private hospitals and clinics. ‘Baby gender tests’ using NIPT techniques are also available to women in the UK on a direct-to-consumer basis from at least three websites for a cost of approximately £170. Finding out the sex of the fetus can sometimes help to determine whether it has inherited a sex-linked genetic condition from the mother if she is a known carrier (see Paragraph 3.6). For many women, however, finding out the sex of the fetus is likely to be motivated by a desire to prepare for a baby of one sex or the other, to bond with the fetus in the womb, or simply curiosity.
- 4.40 Even so, concerns were raised by respondents to our consultation and survey that the availability of sex determination through private NIPT providers makes it more feasible for women to have a termination of a pregnancy motivated by preferences about fetal sex, due to the earlier availability of the information.

“That NIPT should provide this information with greater certainty and earlier in pregnancy is not a problem in principle. However, in cultures where there is a bias towards male babies, NIPT may contribute to the pursuit of illegal abortion on the grounds of gendercide.” (Christian Medical Fellowship – consultation respondent)

- 4.41 It is not clear-cut as to whether terminating a pregnancy for non-medical reasons relating to the sex of the fetus would be unlawful in all cases. The view of the Department of Health is that termination of a pregnancy on the grounds of sex alone is illegal.³⁴¹ However, in practice, Section 1(1)(a) of the Abortion Act (sometimes referred to as the ‘social ground’) provides wide discretion for doctors to certify the lawfulness of termination in the first trimester.³⁴² Obtaining a termination on this ground after 18-20 weeks of pregnancy, the time at which couples can currently find out the sex of the fetus, is more difficult.³⁴³
- 4.42 A review carried out by the Department of Health in 2015 found no substantiated concerns about sex selective abortions occurring in England, Wales and Scotland.³⁴⁴ This might be expected, given that the preference for sons is weak in Western

³⁴¹ Department of Health (2015) *Assessment of termination of pregnancy on grounds of the sex of the foetus - Response to Serious Crime Act 2015* available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/456642/sex_selection_doc.pdf, Sheldon S (2012) Abortion for reason of sex: correcting some basic misunderstandings of the law *Abortion Review* 37: 2.

³⁴² Section 1(1)(a) states “the pregnancy has not exceeded its twenty-fourth week and that the continuance of the pregnancy would involve risk, greater than if the pregnancy were terminated, of injury to the physical or mental health of the pregnant woman”. Furthermore, some have highlighted hypothetical examples in which information about fetal sex might indirectly impact so profoundly on the mental health of the pregnant woman that it would mean criteria set out in Section 1(1)(a) were met. (Sheldon S (2012) Abortion for reason of sex: correcting some basic misunderstandings of the law *Abortion Review*).

³⁴³ Statistics for abortions carried out at or around 18-20 weeks’ of pregnancy are not available but, in 2015, 92 per cent of abortions were carried out before 13 weeks and only one abortion at 24 weeks + 0 days was performed under section 1(1)(a) because of pregnancy complications. See Department of Health (2016) *Abortion statistics, England and Wales: 2015*, available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/570040/Updated_Abortion_Statistics_2015.pdf

³⁴⁴ Department of Health (2015) *Assessment of termination of pregnancy on grounds of the sex of the foetus - Response to Serious Crime Act 2015* available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/456642/sex_selection_doc.pdf.

countries.³⁴⁵ Other research, however, found a significant increase in the ratio of male to female babies of mothers born in India and living in the UK between 1969 and 2005, suggesting that sex-selective terminations have been occurring within this group.³⁴⁶

- 4.43 There is debate about whether it is wrong for people to try to influence or select the sex of their future children for non-medical reasons. The method of sex selection appears to be important, with termination of pregnancy generally being less acceptable to people than preconception methods such as preimplantation genetic diagnosis or sperm sorting (which, nevertheless, are not permitted in the UK for sex selection for non-medical reasons).³⁴⁷ One reason for opposing sex selection by any method is the fear that it will have harmful societal consequences, such as a skewed population ratio that might arise from the preference for male children embedded in certain cultures. Variations in the expected male:female ratio within populations have been used to infer the occurrence of sex selective terminations.³⁴⁸ For example, prenatal sex selection has been suggested as a cause of skewed population ratios in China, South Korea, parts of India and among Indian communities in Canada and the USA.³⁴⁹
- 4.44 Another reason that some people oppose sex selection practices is the belief that they are sexist and wrongly involve assigning greater value to one sex than the other, and can also encourage sexism and discrimination more widely.³⁵⁰ Allowing such practices, therefore, might be in tension with other state policies aiming to address sex discrimination and to make society more equal for men and women. Others argue that it is speculative to assume that preferences for a child of a given sex are always sexist, and suggest that it is possible for people to want a child of one sex without believing that sex to be superior to the other. They may instead value the kind of relationship they think they would form with a child of that sex. Alternatively, their reasons may be related to 'family balancing' and the desire to have a family that is made up of children of different sexes.³⁵¹ However, even when prospective parents anticipate having a certain kind of relationship with either a son or daughter, or want a child of one sex for family balancing reasons, it is likely that these preferences will stem from fixed ideas about males and females.
- 4.45 There may be other reasons for restricting access to information about the sex of the fetus, even in cases where women and couples are simply curious or want to prepare for a baby of one sex or the other. Firstly, unless sex determination is being used to

³⁴⁵ Van Balen F (2006) Attitudes towards sex selection in the western world *Prenatal diagnosis* **26**: 614-8.

³⁴⁶ Dubuc S and Coleman D (2007) An Increase in the Sex Ratio of Births to India-born Mothers in England and Wales: Evidence for Sex-Selective Abortion *Population and Development Review* **33**: 383-400.

³⁴⁷ Human Fertilisation and Embryology Authority (2003) *A report on the HFEA's 2002-03 review of sex selection including a discussion of legislative and regulatory options*, available at: http://www.hfea.gov.uk/docs/Final_sex_selection_main_report.pdf.

³⁴⁸ Caird J, Brunton G, Stokes G et al. (2015) *Sex-selective abortion: a systematic map of the volume and nature of research*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/456641/SSA_Systematic_map_report.pdf.

³⁴⁹ Urquia ML, Ray JG, Wanigaratne S, Moineddin R and O'Campo PJ (2016) Variations in male-female infant ratios among births to Canadian- and Indian-born mothers, 1990-2011: a population-based register study *Canadian Medical Association Journal Open* **4**: E116-E23; Hesketh T, Lu L and Xing ZW (2011) The consequences of son preference and sex-selective abortion in China and other Asian countries *Canadian Medical Association Journal* **183**: 1374-7; Puri S, Adams V, Ivey S and Nachtigall RD (2011) "There is such a thing as too many daughters, but not too many sons": A qualitative study of son preference and fetal sex selection among Indian immigrants in the United States *Social Science and Medicine* **72**: 1169-76.

³⁵⁰ Dondorp W, De Wert G, Pennings G et al. (2013) ESHRE Task Force on ethics and Law 20: sex selection for non-medical reasons *Human Reproduction* **28**: 1448-54.

³⁵¹ Wilkinson S and Garrard E (2013) *Eugenics and the ethics of selective reproduction*, available at: <https://www.keele.ac.uk/media/keeleuniversity/ri/risocsci/eugenics2013/Eugenics%20and%20the%20ethics%20of%20selective%20reproduction%20Low%20Res.pdf>.

diagnose a sex-linked medical condition, it has no clinical utility. Healthcare professionals involved in the provision of NIPT should meet the standards set by their professional bodies to both respect the rights and wishes of individual patients *and* to ensure all patients receive good care and treatment. Offering tests that have no clinical utility could be regarded as not meeting their responsibilities in this regard (see Paragraph 1.44). Furthermore, whilst some women and couples may feel that knowing the sex of the fetus would help them to bond with their future child it is not clear that this means that they should be able access this information at nine to ten weeks of pregnancy rather than at the 18-20 scan.

- 4.46 In addition, it has been argued that potential parents are interested in finding out about the *gender* of their future child i.e. the socially constructed roles, behaviours, activities and attributes that a given society considers appropriate for men and women – and that knowing the sex of the fetus will not provide them with this information.³⁵² Finding out the sex of a fetus prenatally may reinforce parents' expectations about their future child's interests and tendencies as determined by gender, and these expectations may harm a child's development.³⁵³ It is unclear, however, whether the offer of sex determination using NIPT would make any difference in this regard, given that women already can find out the sex of the fetus a few weeks later at the 18-20 week scan, and certainly at birth.
- 4.47 In recognition that sex selection is a serious issue in India and China, both ethically and demographically, it is illegal in both countries to terminate pregnancies on the grounds of sex and to identify fetal sex and give the information to the family.³⁵⁴ In countries where prenatal sex determination is legal, such as North America, there is evidence that population subgroups drawn from those regions are using prenatal sex determination to inform sex selective terminations.³⁵⁵ We also heard reports that countries where prenatal sex determination is legal, such as Hong Kong, are becoming destinations for 'sex selection tourism' for people from neighbouring countries.³⁵⁶
- 4.48 The question should be asked whether concerns about sex selective terminations and lack of clinical utility warrant imposing any restrictions on access to information about sex using NIPT in the UK. Imposing such restrictions may be ineffective at preventing sex selective terminations given the possibility of accessing NIPT services in other countries or via the internet and the fact that it appears that sex selection took place in some ethnic groups in the UK before NIPT was available. In addition, allowing women and couples to access NIPT for sex determination within healthcare settings in the UK may maximise the chances of people receiving good information and counselling along with test results. There is limited evidence that sex selective terminations are taking place in the UK, but it is likely that the use of NIPT in the private sector has increased since this evidence was gathered, and it is unknown whether this has led to or will lead to an increase in sex selective terminations. There is a real possibility that permitting NIPT for sex determination in the UK may be encouraging sex selection, both among UK residents

³⁵² Browne TK (2017) Why parents should not be told the sex of their fetus: a response to the commentaries *Journal of Medical Ethics* **43**: 19-21.

³⁵³ Kane EW (2017) Sidestepping a trap: a commentary on 'why parents should not be told the sex of their fetus' *Journal of Medical Ethics* **43**: 13; Dondorp W, De Wert G, Pennings G *et al.* (2013) ESHRE Task Force on ethics and Law 20: sex selection for non-medical reasons *Human Reproduction* **28**: 1448-54.

³⁵⁴ Chandrasekharan S, Minear MA, Hung A and Allyse MA (2014) Noninvasive Prenatal Testing Goes Global *Science Translational Medicine* **6**: 231fs15-fs15; Ahankari AS, Myles P, Tata LJ and Fogarty AW (2015) Banning of fetal sex determination and changes in sex ratio in India *The Lancet Global Health* **3**: e523-4.

³⁵⁵ Puri S, Adams V, Ivey S and Nachtigall RD (2011) "There is such a thing as too many daughters, but not too many sons": A qualitative study of son preference and fetal sex selection among Indian immigrants in the United States *Social Science and Medicine* **72**: 1169-76.

³⁵⁶ South China Morning Post (2012) *Mums-to-be in rush for fetus sex tests*, available at: <http://www.scmp.com/news/china/article/1051897/mums-be-rush-fetus-sex-tests>.

and through 'sex selection tourism'. The Department of Health acknowledges this: "The emergence of NIPT testing underlines the need for us to continue to monitor birth ratios and abortion data by ethnicity to monitor whether the availability of new tests may be having an impact, particularly if they become more widely available."³⁵⁷

Potential future developments

- 4.49 It is already possible for pregnant women to access NIPT for quite a number of genetic conditions and traits through the private sector, and most manufacturers offer to test for at least one non-medical trait i.e. sex. It appears that some NIPT manufacturers believe offering to test for more genetic conditions and traits is attractive to potential customers. As manufacturers compete with each other for their share of market, it is possible that the trend of offering NIPT for more conditions and traits will continue. It is an important moment, therefore, to consider whether this expansion should continue unchecked.

Test performance

- 4.50 If any future test performs poorly, and does not give a woman an accurate and reliable prediction of whether their fetus has the condition or trait being tested for, this could undermine her ability to make informed reproductive choices, lead more women to have invasive diagnostic procedures, and would constitute a poor or unacceptable healthcare service. The current offer of NIPT for certain microdeletions, which have unknown or poor test accuracy, might fall into this category (see Paragraph 1.29). It is not straightforward to define what would constitute an accurate and reliable test, however. The acceptable thresholds of the different components of test accuracy (i.e. sensitivity, specificity, positive predictive value and negative predictive value) are likely to be different for each condition being tested for. For example, if a condition was rare but fatal without immediate treatment, it would be important to identify all fetuses with the condition, so high test sensitivity would be desirable and false positives might be thought to be less problematic. A less serious condition with fewer immediate outcomes would allow more time and opportunity for detection and so the level of false positives would need to be weighed against the likelihood of missing some fetuses with the condition. To enable women to make informed and autonomous choices, healthcare professionals have a responsibility to ensure that any new test is provided alongside information and support that is balanced, accurate and non-directive. It is essential that information about the accuracy of the test and the likelihood of a false result is available, and that women and couples have the information they need to make an informed choice about whether or not to have the test.

NIPT for less significant medical conditions and non-medical traits

- 4.51 We asked survey respondents what kind of genetic information pregnant women and couples should be able to find out about their fetus. In general, respondents were much more supportive of pregnant women and couples being able to find out about significant medical conditions that result in death before or shortly after birth, conditions that affect the child early in life and conditions for which there is no treatment, than they were of less significant medical conditions, conditions for which there is effective treatment and conditions that manifest in adulthood. There was very little support for allowing women

³⁵⁷ Department of Health (2015) *Assessment of termination of pregnancy on grounds of the sex of the foetus - Response to Serious Crime Act 2015* available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/456642/sex_selection_doc.pdf.

and couples to find out prenatally information relating to the physical appearance of the future child or other non-medical characteristics. Some were concerned about diversity and tolerance in society and that people may make use of NIPT to enable them to have 'designer babies'.

"The only genetic information which can be of any real use for parents is that which can lead to therapeutic (life-affirming) intervention, at the optimum time." (Saving Down Syndrome – consultation respondent)

"I feel this technology will be abused to the point where humans will be 'designed' in a certain way." (Person with a family member or close friend with a genetic condition – survey respondent)

4.52 As discussed throughout this report, accessing NIPT for significant medical conditions or impairments can enable pregnant women and couples to make informed choices about their pregnancies regarding whether to continue and prepare for the birth of a disabled child or whether to have a termination. Accessing NIPT for less significant medical conditions, or non-medical traits, such as sex, eye colour, height or sporting ability in the normal range (i.e. traits that generally would not be considered ground for termination), may also provide pregnant women with information about their fetus and future child to which they may feel they have a right. It may help them prepare psychologically and practically for the birth of a baby with a genetic condition or a particular trait. It is already possible to access NIPT in the private sector for sex determination, as discussed above, and for some conditions that might not always be considered to be significant medical conditions or impairments, such as triple X syndrome. However, allowing pregnant women and couples access to NIPT for less significant medical conditions or non-medical traits raises a number of concerns, which we will now discuss in turn (issues raised regarding the possible future use of NIPT to test for adult onset conditions and carrier status are discussed in Chapter 3).

4.53 The first concern relates to the lack of clinical utility of NIPT for these conditions or traits. This kind of NIPT would not offer information that would benefit the health of the woman, fetus or future person, nor inform reproductive decisions. For this reason, NIPT for less significant medical conditions and non-medical traits is unlikely ever to be offered within the NHS. Within the private sector however, some argue that women have a right to access any available information about themselves and their fetus if they so wish and have the financial means, regardless of its usefulness, and to restrict access to this information would be problematic. Some respondents to our survey shared this view:

"I think denying women information that exists about health conditions they will have to contend with should never be withheld. It is denying choice and wholly unethical." (Person with multiple interests in NIPT – survey respondent³⁵⁸)

"Anything that helps a parent prepare for the birth of their baby should be encouraged." (Person with a family member or close friend with a genetic condition – survey respondent)

4.54 However, given the standards in the provision of information and support to women undergoing NIPT that we suggested earlier in the report should be upheld, the Working Group is of the view that NIPT should always be offered in healthcare settings and/or under the guidance and support of skilled healthcare professionals. Given this, NIPT

³⁵⁸ Survey respondent with recent experience of being pregnant, a general professional interest in prenatal screening, a family member or close friend with a genetic condition and a general interest in NIPT.

should be categorised as healthcare, and the practice of healthcare professionals involved in the provision of NIPT should meet the standards set by their professional regulator and bodies to both respect the rights and wishes of individual patients *and* to ensure that all patients receive good care and treatment (see Paragraph 1.44). Offering tests that have no clinical utility could be regarded as not meeting these responsibilities. Where NIPT is offered on a direct-to-consumer basis (as with ‘baby gender tests’ that can be purchased over the internet and involve a prick of the finger that the woman performs herself), its provision less closely resembles a healthcare service and is more like any other consumable product. However, if the information on offer is not relevant to the woman’s reproductive autonomy, i.e. to decisions she may wish to make about her pregnancy, it is questionable that she has a right to all information of this nature.³⁵⁹

- 4.55 A further concern related to NIPT for less significant medical traits or non-medical conditions is that it is possible that women who obtain information of this kind so early in pregnancy may be motivated to seek terminations under Section 1(1)(a) of the Abortion Act, as discussed above in the case of sex determination. Potential harms arising from selective terminations of this kind include imbalances in the population, encouraging discrimination against people with certain genetic traits, and treating children as commodities or failing to accept them as ‘gifts’.³⁶⁰ Such practices may also threaten the biological benefits conveyed by genetic diversity in the human species. Variety in the gene pool of a species allows greater opportunity for adaptation in changing environments for the species as a whole, and these can bestow both favourable and unfavourable survival characteristics on individuals within that species as a consequence.³⁶¹ It is also possible that access to information about a much broader range of fetal traits might, over time, alter perceptions of healthiness and raise the threshold of what is considered to constitute a ‘normal’ or ‘healthy’ baby.³⁶² A number of survey and consultation respondents raised concerns about this, sometimes in relation to eugenics, in the context of use of NIPT for less serious medical conditions and non-medical traits. The Nuffield Council on Bioethics has previously concluded that the use of selective termination following prenatal diagnosis of behavioural traits in the normal range is morally unacceptable.³⁶³

“...it is a gradual step towards eugenics where abortion is seen as a solution to a social or cultural situation. This has a significant impact on populations, social attitudes etc. and should not be encouraged.” (Person with experience of undergoing NIPT – survey respondent³⁶⁴)

³⁵⁹ Feinberg J (1980) The child’s right to an open future, in *Whose child? Children’s rights, parental authority and state power*, Aiken W and LaFollette H (Editors) (US: Rowman and Littlefield) and Davis DS (1997) Genetic dilemmas and the child’s right to an open future *Hastings Center Report* 27: 7-15.

³⁶⁰ Sandel MJ (2009) *The case against perfection* (Harvard: Harvard University Press); Scully JL, Shakespeare T and Banks S (2006) Gift not commodity? Lay people deliberating social sex selection *Sociology of Health & Illness* 28: 749-67.

³⁶¹ National Institutes of Health (US) (2007) *Biological sciences curriculum study. NIH curriculum supplement series. Understanding human genetic variation.*, available at: <https://www.ncbi.nlm.nih.gov/books/NBK20363/>; Balaresque PL, Ballereau SJ and Jobling MA (2007) Challenges in human genetic diversity: demographic history and adaptation *Human Molecular Genetics* 16: R134-R9.

³⁶² Ma Y, Gong H and Wen Y (2013) Nucleic acid-based non-invasive prenatal diagnosis of genetic skin diseases: are we ready? *Experimental Dermatology* 22: 392-5; Kent A (2008) Non-invasive prenatal diagnosis: Public and patient perceptions *Seminars in Fetal and Neonatal Medicine* 13: 109-12.

³⁶³ Nuffield Council on Bioethics (2002) *Genetics and human behaviour: the ethical context*, available at: <http://nuffieldbioethics.org/wp-content/uploads/2014/07/Genetics-and-human-behaviour.pdf>.

³⁶⁴ Survey respondent with recent experience of being pregnant and a family member or close friend with a genetic condition.

“Screening can be a slippery slope to eugenics if not tightly controlled and handled with current up to date examples, information and neutrality.” (Person with a family member or close friend with a genetic condition - survey respondent)

- 4.56 Another argument against allowing women and couples to access NIPT for some less significant medical conditions and non-medical traits is that there is value in enabling future people to make their own decisions about accessing their genetic information. Use of NIPT for these purposes before birth might undermine prospects for the person that the fetus might become to make their own autonomous choices. Sometimes this is described in terms of the fetus having a right to an open future, which would be a right held ‘in trust’ that could be violated in advance by the use of NIPT to identify genetic information about them. The extent of any right to an open future has been contested in the context of children’s rights by some who query how ‘open’ people are obliged to leave the future of their children.³⁶⁵ Given that parental decisions inevitably shape the course of their children’s lives some have argued that it is not possible, in any meaningful way, to keep children’s options open. Nevertheless, some of our survey respondents were concerned about this issue in the context of prenatal genetic testing

“It also means the child in the future [would] not have the ability to make their own decisions regarding discovering whether they have any medical conditions that could affect them for life.” (Person with multiple interests in NIPT - survey respondent³⁶⁶)

- 4.57 Future people might also be psychologically affected, and feel limited, by information that is available to them about less significant medical conditions and traits they might have or develop. They might take their options for education, employment, housing, lifestyle and other areas to be constrained by this knowledge. It has been suggested that the experiences of children about whom this kind of genetic information is available might include possible lessened self-esteem, distortion of the family’s perception of the child, altered upbringing, discrimination and increased anxiety both of parent and child.³⁶⁷ Alternatively, some individuals may respond to such information in more positive ways and may be motivated to defeat what they might see as challenges to be overcome. Use of NIPT to access this kind of information might also cause harm by shutting down possibilities for the people that fetuses might become. For example, if insurance companies or employers were able to gain access to genetic information that had been obtained through NIPT, those with certain genetic profiles might find it more difficult to access certain goods and services, and would be worse off as a result. A survey respondent raised this as a concern:

“There will be demands from insurers for people to release the information which may well make it harder for people to obtain insurance or mortgages.” (Person with multiple interests - survey respondent³⁶⁸)

- 4.58 Professional guidance has recommended that genetic testing of children that is primarily predictive of future impairment or reproductive risks, as opposed to informing immediate

³⁶⁵ Wilkinson S (2012) *Choosing Tomorrow’s Children: The Ethics of Selective Reproduction* (Oxford: Oxford University Press); Mills C (2003) The Child’s Right to an Open Future? *Journal of Social Philosophy* 34: 499-509.

³⁶⁶ Survey respondent with experience of undergoing NIPT and a family member or close friend with a genetic condition.

³⁶⁷ It has been observed that there is a lack of evidence in these areas. For discussion, see British Society for Human Genetics (2010) *Report on the genetic testing of children 2010*, available at: http://www.bsgm.org.uk/media/678741/gtoc_booklet_final_new.pdf.

³⁶⁸ *ibid.*

³⁶⁸ Person with a family member or close friend with a genetic condition and with experience of undergoing NIPT.

medical care, should normally be delayed until the young person can decide for him/herself when, or whether, to be tested.³⁶⁹

- 4.59 Obtaining information about less significant medical conditions and non-medical traits through NIPT may not always result in the harms to the future person suggested above to the same extent. For example, prenatal testing for traits that are usually obvious at birth or soon into childhood, such as sex, eye colour or minor birth defects or deformities, is likely to have little impact on the capabilities, privacy or rights of the future person. On the other hand, testing for behavioural traits such as intelligence, susceptibility to aggression and other antisocial conduct, could very well harm the future person that the fetus may become, if testing for these traits becomes available in the future.

NIPT for whole genome or exome sequencing

- 4.60 If whole genome or exome sequencing using NIPT were to become available commercially in the future, pregnant women or couples would have access to any interpretable genetic information about their fetus, as well as a large amount of information of unknown significance. The arguments set out previously in relation to NIPT for information of unknown significance, adult onset conditions, carrier status, less significant medical conditions or impairments, and non-medical traits apply here as well (see Paragraphs 3.33-3.39 and 4.51-4.59). Any restrictions on access to information about the fetus would also need to apply to whole genome or exome sequencing, otherwise these restrictions could be by-passed.
- 4.61 In the context of NHS prenatal genetic testing in women with a known risk of developing a condition, professional guidelines suggest that targeted testing is preferred where possible to reduce the potential for results with unclear clinical significance and/or the generation of unanticipated or secondary findings (see Paragraph 3.15). Most respondents to the consultation held similar views about the possibility of whole genome sequencing becoming available commercially. There was concern about the difficulty of interpreting the information that would result from whole genome sequencing, the anxiety this might cause pregnant women and couples, and the lack of clinical utility of the majority of the information. Concerns were also raised about the potential impact of prenatal whole genome sequencing on the rights of the future person that the fetus may become, and that the information arising from whole genome sequencing would be highly sensitive, raising issues relating to privacy, data protection and storage.

“Until we know the full extent of genes it could lead to worry.” (Person with a family member or close friend with a genetic condition - survey respondent)

“Maybe people should have the right to decide for themselves if they want this later in life when they can make their own decisions.” (Person with multiple interests in NIPT - survey respondent³⁷⁰)

³⁶⁹ British Society for Human Genetics (2010) *Report on the genetic testing of children 2010*, available at: http://www.bsgm.org.uk/media/678741/gtoc_booklet_final_new.pdf.

³⁷⁰ Survey respondent with a family member or close friend with a genetic condition, and recent experience of being pregnant.

Chapter 5

Ethical values and NIPT

Chapter 5 – Ethical values and NIPT

Chapter overview

The issues raised by non-invasive prenatal testing (NIPT) can be cast within a framework based on the values of choice, autonomy and consent; avoidance of harm; and equality, fairness and inclusion. These values may be promoted or undermined by NIPT in different ways for women and couples, people that fetuses might become, and disabled people. Perspectives on whether, and to what extent, a fetus also has interests that may be harmed by NIPT depend on views about the moral status of the fetus.

Choice, autonomy and consent – NIPT can enhance reproductive autonomy in different ways, including by enabling women and couples to prepare for a baby with a genetic condition or impairment, or to decide to have a termination, potentially at an earlier stage of pregnancy. However, NIPT can undermine autonomy and choice if accurate and balanced information about the test and the conditions being tested for is not available, or if women and couples feel that they are expected to make a particular decision, and by posing risks to the personal autonomy of the future people that fetuses might become.

Avoidance of harm – NIPT has the potential to reduce harms to pregnant women and fetuses, such as where it can replace or reduce the need for invasive testing. However, NIPT could lead to anxiety and more invasive procedures where inaccurate or unreliable results are returned. If NIPT leads to a significant decrease in the number of people born and living with genetic conditions or impairments, it could lead to fewer resources being invested in research and health and social care relating to people with genetic conditions, and cause offence and social isolation.

Equality, fairness and inclusion – NIPT has the potential to enhance the ability of women to choose the circumstances of their pregnancy, helping to promote equality for women more generally. However, NIPT may give rise to perceptions that people are 'to blame' for having a baby with a disability, may change views about what is considered to be a healthy pregnancy or child, and may make disabled people and their families more vulnerable to stigma, discrimination and abuse.

An ethical approach

The tensions that exist between the potential benefits and the risks of NIPT, and between the ethical values to which they relate, create challenges for public policy. The Working Group suggests three general principles, which should always be considered together, to guide policy making in relation to NIPT:

- **Principle 1.** The wider societal environment in which NIPT is provided and developed should be considered when developing policy relating to NIPT.
- **Principle 2.** Pregnant women and couples should have access, where appropriate, to NIPT within an environment that enables them to make autonomous, informed choices.
- **Principle 3.** Efforts should be made to reduce any risks of significant harms posed by the growing use and development of NIPT.

Introduction

- 5.1 In this chapter, we summarise the ethical issues that have been raised in relation to different uses of non-invasive prenatal testing (NIPT) either by the people and organisations we consulted with during the project, or in the academic literature. Many relate to current uses of NIPT, others relate to potential future uses of the technique. We suggest that the issues raised by NIPT can be cast within a framework based on the values that we set out in Chapter 1, namely: choice, autonomy and consent; avoidance of harm; and equality, fairness and inclusion. We then suggest an ‘ethical approach’ to the development of public policy relating to NIPT.
- 5.2 Our summary sets out the moral impact that NIPT may have on different groups (including women and couples, people that fetuses might become and disabled people). This raises a question about whether, and to what extent, a fetus also has interests that may be harmed or wronged. Perspectives on this are likely to depend on views about the moral status of the fetus and there are broadly three positions that a person might adopt with respect to this question.³⁷¹ The fetus might be accorded full moral status and therefore considered to be owed maximal moral regard or duties. Alternatively, the fetus might be accorded no moral status and therefore considered to be owed no direct moral duties. The fetus might also be accorded partial or limited moral status, and therefore owed direct but not maximal moral duties. The latter view is consistent with proportional or gradualist positions, which hold that the weight of the regard or duties directly owed to the fetus increases during gestation. Perspectives that accord the fetus proportional moral status imply that there are ethical benefits from enabling terminations to take place earlier and, conversely, that terminations are more ethically problematic when they take place later. Those who believe that the fetus has full moral status are more likely to hold a view that termination is almost always harmful or wrong and, conversely, those who believe that the fetus has no moral status are more inclined to view termination as morally unproblematic. In the UK, a fetus is not a legal person, but is accorded legal protection by various laws. Review of these laws, including the Abortion Act 1967, is outside the remit of this project (for more detail, see Paragraphs 1.49-1.53).

Choice, autonomy and consent

- 5.3 NIPT as a prenatal test of superior safety (as compared to invasive diagnostic tests) and accuracy (as compared to other screening tests) offers the prospect of enhanced reproductive autonomy to pregnant women and couples. However, the development of and widening access to NIPT might either support or undermine choice in different ways for pregnant women and couples, future people that fetuses might become, disabled people, and wider society. For example, NIPT may offer opportunities for better-informed decision making for women, but also raises issues relating to ‘routinisation’ and informed consent, amongst other issues. The following section maps out the potential benefits and ethical concerns raised by NIPT in the context of supporting choice, and how they relate to different groups.

³⁷¹ Pattinson SD (2014) *Medical Law and Ethics* (London: Sweet & Maxwell).

Pregnant women and couples' reproductive choices

5.4 We have seen that NIPT has the potential to enhance or facilitate reproductive choice for pregnant women and couples in different ways, including:

- Enabling preparation: if NIPT provides an accurate and reliable prediction of whether the fetus has or does not have the condition being tested for, this can be helpful in informing decisions about different options for clinical interventions during pregnancy and enabling women and couples to prepare psychologically and practically for the birth of a disabled child.
- Informing decisions about termination: women might also benefit from accessing such information to help them make decisions about whether to continue a pregnancy, or terminate it and so avoid having a child with a significant medical condition or impairment.
- Enabling earlier choices: NIPT can be carried out from approximately nine or ten weeks of pregnancy, meaning that women can have access to information about their pregnancy earlier than through existing prenatal screening and testing methods.
- 'For information only': women and couples might benefit from being able to choose to find out information about the fetus 'for information only', rather than as a tool to inform decision making in pregnancy. For example, finding out fetal sex might enhance the experience of pregnancy for prospective parents and support bonding with an unborn baby. Some believe that parents have a moral right to choose to find out genetic information about their fetus and future child.

5.5 However, NIPT also has the potential to undermine or threaten the reproductive choices of pregnant women and couples, particularly in relation to the way in which NIPT is offered or delivered in different ways, including:

- Pressure to undergo NIPT and the 'right not to know': the less invasive nature of NIPT as compared with amniocentesis and chorionic villus sampling (CVS) raises the possibility that NIPT might come to be seen as a routine or standard part of maternity care. This might influence medical and societal perspectives on screening and testing, and create an expectation that women will undergo NIPT. It may also expose women to pressure, which could make it more difficult for them to choose not to undergo screening.
- Threats to the quality of informed consent: as a blood test with minimal associated physical risks, there are concerns that NIPT might not involve the same level of explanation and discussion as invasive testing, undermining the prospects for women to be in a position to make informed decisions about NIPT.
- Inaccurate or unreliable results: NIPT that does not provide an accurate and reliable prediction of whether the fetus has or does not have the condition being tested for could undermine the ability of women and couples to make informed reproductive choices.
- Quality of information about disability: inaccurate or out-of-date understandings of the impacts on disabled people and their families of genetic variations, and broader unduly negative medical or societal attitudes towards disability, may be more detrimental to genuine reproductive choice if NIPT screening is viewed as 'easier'.

The choices of future people (i.e. those born to parents who have used NIPT)

- 5.6 If NIPT for a wider range of genetic conditions and traits becomes available in future, NIPT might pose risks to the autonomy of those people whose genetic material was tested while they had been in their mother's womb. Usually, it is regarded as a personal choice whether or not to undergo genetic testing that could provide information about a person, including about adult onset conditions, carrier status, less significant medical conditions or non-medical conditions. It is arguably wrong to arrange a genetic test before birth because it deprives a person of her or his opportunity to make their own autonomous decision about whether to undergo testing or might undermine their right to an open future.

The choices of disabled people

- 5.7 NIPT might enhance the reproductive autonomy of people without or with a family history of a significant medical condition or impairment who do not want their children to inherit the condition. It might also help disabled people who are concerned about the impacts on existing children of having a disabled sibling or who feel that their own disability would make it difficult or impossible for them to raise a disabled child.

Avoidance of harm

- 5.8 The potential for NIPT to either reduce or give rise to harms in different groups in different contexts is of key importance when appraising the ethical issues connected with NIPT. Pregnant women and couples, the fetus, the future people that fetuses may become, disabled people and healthcare professionals might experience different kinds of harms and benefits from the increasing use of the technique.

Harms to pregnant women and couples

- 5.9 NIPT has the potential to reduce harms to pregnant women and couples in several ways, including:
- Avoiding the risks of invasive testing: for some conditions and under some circumstances, NIPT is as accurate as invasive testing, avoiding the need to have invasive testing altogether. For other conditions, NIPT has a lower rate of false positive results than other screening tests, meaning fewer women will be exposed to the risk of miscarriage and the discomfort associated with invasive tests.
 - More accurate results: NIPT is more accurate than other screening tests for some conditions, meaning fewer women will receive false positive or false negative results and will experience less of the anxiety associated with making decisions about undergoing invasive tests.
 - Avoiding harms of late terminations: some research suggests that second trimester terminations are associated with higher levels of stress for women than first trimester terminations, at least in the short term. Where the combined test and NIPT is more accurate than the combined test alone, fewer fetuses with Down's, Edwards' or Patau's syndromes may be missed at this stage only to be discovered by screening or testing being carried out later in pregnancy, potentially meaning some later terminations are avoided.

5.10 NIPT also has the potential to give rise to harms to pregnant women and couples in several ways, again particularly in relation to the way in which NIPT is offered or delivered, including:

- Misleading promotional materials: we have seen examples of marketing materials produced by private NIPT providers that could be considered to exploit women and to play on the anxieties and fears that couples may have about pregnancy. These include materials that misleadingly promise reassurance to women and couples, or incorrectly state or imply that NIPT can exclude the possibility that certain fetal anomalies are present. This might lead to psychological harms, as well as raising financial or consumer issues for those who seek NIPT under false impressions about the nature of the test.
- Absence of support and counselling: if NIPT is offered without appropriate support, advice and guidance this might mean that women and couples experience greater levels of psychological distress or anxiety following receipt of NIPT results, or mistakenly take NIPT to be diagnostic in cases where it is not.
- Inaccurate or unreliable results: NIPT that does not provide an accurate and reliable prediction of whether the fetus has or does not have the condition being tested for might cause unnecessary anxiety and lead more women to have invasive diagnostic procedures.
- The potential for unanticipated or secondary findings: NIPT can reveal information about the woman's own health, including clinically relevant genetic information and cancerous and malignant tumours. This could present benefits for women, in that treatment can be sought. However, if the implications of these findings are not well understood or the possibility of unanticipated or secondary findings is not discussed with women before they undergo NIPT, there could be negative psychological impacts when findings of this sort are returned and challenges for healthcare professionals when giving women NIPT results.
- Harms of later diagnoses: in the case of NIPT for Down's, Edward's and Patau's syndromes, introducing it as a second stage screening test might delay diagnosis for some women, and may give rise to delays in women accessing terminations.
- Failed or inconclusive tests: with all NIPT, there is the possibility of test failure or inconclusive test results. This varies depending on several factors but has been found to vary from 0 to 13 per cent (see Paragraph 1.20). Women who have a failed test may need to undergo further testing to get a result. Anxiety can be created by delays and there may be financial and consumer issues for women who have sought NIPT in the private sector.
- Psychological impact of terminations: deciding to terminate a pregnancy following a diagnosis of fetal anomaly is frequently described by pregnant women and couples as distressing, particularly if this takes place in the second trimester, with some reporting feeling unprepared for making such a decision. However, it has been shown that in the majority of women adverse psychological effects reduce over time and few women report feelings of regret over their decision to have a termination.

Harms to fetuses

5.11 NIPT might reduce harms to fetuses in a number of ways, including:

- Avoiding the risks of invasive testing: the small risk of miscarriage associated with invasive testing can be viewed as posing potential harm to the fetus, as well as to women and couples. Fewer fetuses will be exposed to these risks to the extent that NIPT reduces the need for women to undergo invasive testing in order to find out whether or not the fetus has a given condition.
- Avoiding harms of late termination: those who take a proportional or gradualist view of the fetus are likely to view earlier terminations as less harmful, and less wrong, than later terminations. According to this view, NIPT might provide benefits to the fetus, as well as to women and couples, in terms of potentially reducing the number of fetuses with Down's, Edwards' or Patau's syndrome that are missed during first stage screening but are identified later in pregnancy and result in a later termination.

5.12 NIPT also has the potential to give rise to harms to fetuses:

- Increase in terminations: there are concerns that introducing NIPT in NHS prenatal screening for Down's, Edwards' and Patau's syndromes may result in an increase in the number of terminations of pregnancies affected by these conditions. The potential of NIPT to test for a growing range of conditions and traits might also have implications for the number of pregnancies that are terminated in the future. An increase in the overall number of terminations is likely to be considered harmful and wrong by those who believe that the fetus has full moral status or has reached the point of having partial moral status.

Harms to future people (i.e. those born to parents who have used NIPT)

5.13 If NIPT for a wider range of genetic conditions and traits becomes available in future, NIPT might give rise to harms to future people in a number of ways, including:

- Closing down of life options: people may feel limited by the information they now have about their health. People might take their options for education, employment, housing, lifestyle and other areas to be constrained by the knowledge that they might develop certain health conditions. It is also possible that other people, organisations or institutions might actively restrict access to opportunities and services for people with particular genetic profiles including in areas relating to employment, life and health insurance, education and state provided services.
- Negative psychological impact of knowledge of adult onset conditions: children and adults with an adult onset medical condition or impairment identified before their birth by NIPT would be required to live for much of their lives with the knowledge that it is likely that they will develop a condition or impairment later in life, if their parents disclose these results to them. Many adults who are at risk of adult onset conditions prefer not to know.
- Privacy violations: people might be wronged by others having access to personal information that was obtained about them through NIPT. They may benefit from being able to exercise control over who can access this information and being able to make

their own decisions about whether other people, including family members, know about health conditions and other genetic traits they have or might develop.

Harms to disabled people

5.14 NIPT might give rise to harms to people with the conditions and impairments that NIPT is used to test for in a number of ways, including:

- Psychological harms: the increasing availability and use of NIPT might cause or exacerbate psychological harms to people with genetic conditions or impairments who may view prenatal testing or screening as expressing a negative view or judgment about the value of disabled people in general and the value of their lives in particular.
- Less investment in research and support: as NIPT technology develops, it might be perceived by funders and charities conducting research into, and providing services for people with genetic conditions and impairments that there is less need to research, develop treatments, or provide support for such people. This could impact on the levels of available support in the long term.
- Reduction in the population of people with a given genetic condition or disability: it is possible that the improved safety and accuracy of NIPT may result in greater screening uptake in the future. This may mean that terminations increase, which could in turn result in the incidence or prevalence of people with a given genetic condition or impairment declining. This might be considered by people with that condition to be bad in and of itself if, for example, there were fewer people who are able to share experiences of living with particular genetic variations. This might give rise to social isolation and cause or exacerbate other harms, such as less research, fewer services, or more discrimination.

Harms to healthcare professionals

5.15 One way in which NIPT might give rise to harms to healthcare professionals is in the area of conscientious objection. NIPT might be perceived to exacerbate existing challenges for healthcare professionals who have conscientious objections to prenatal screening and termination. There remains uncertainty about the implications of the introduction of NIPT in the NHS, and therefore it is unclear whether NIPT will present any distinctive or novel problems for NHS healthcare professionals who have ethical objections to prenatal screening and termination.

Equality, fairness and inclusion

5.16 The wider societal effects of the growing use of NIPT, and the prospective development of the technique to detect other kinds of genetic traits, are important aspects of the ethical considerations raised by NIPT. It is possible that NIPT might support or undermine efforts to promote equality, fairness and inclusion in different ways for women, disabled people and throughout society more generally. Inequality, unfairness and exclusion could be harmful to different parties but might also be wrong independently of any harms they cause.

Equality, fairness and inclusion for women and couples

5.17 NIPT has the potential to enhance and undermine equality, fairness and inclusion for women and couples in a number of ways, including:

- **Equality for women more generally:** NIPT may enhance the ability of women to exercise control over the circumstances of parenthood, which could have positive effects on the equality of women in different contexts. The availability of prenatal screening enables women to plan parenthood around other aspects of their lives at times that suit them professionally and in other ways, with potential consequences for their place in the workplace and society more widely. Others may worry that NIPT might create new pressures on women to become parents at stages in their life that were not possible in the past.
- **Equitable access to healthcare:** Making NIPT for screening or testing for some conditions available in the NHS means that women who have been identified as having a higher chance of having a fetus with these conditions will have equal access to safer, more accurate prenatal testing. However, women who are not eligible for NIPT on the NHS, such as those who do not have an increased chance of having a fetus with a genetic condition, would have to pay for NIPT privately if they want to access the benefits of NIPT over other kinds of screening and testing. Women who are financially better off will disproportionately benefit from this availability.

Equality, fairness and inclusion for disabled people

5.18 NIPT has the potential to undermine equality, fairness and inclusion for disabled people in a number of ways, including:

- **Discrimination and stigma:** the availability of NIPT as an accurate and safe screening test might change the way that society views the occurrence of some conditions, and possibly of disability more generally, and some have expressed concerns that it might give rise to perceptions that people are 'to blame' for having a baby with a disability. Such perceptions might make disabled people and their families more vulnerable to discrimination, stigma or abuse. Disapproval of the decisions that families make may encourage the 'privatisation' of disability, from which perspective it may be seen as the family's responsibility to meet the needs of disabled people and no longer as the responsibility of the state.
- **'Screening out' and eugenics:** some have raised concerns that the ease and accuracy of NIPT might result in the widespread uptake of prenatal screening and may ultimately bring about the elimination from society of people with certain conditions. Some argue that this constitutes eugenics and devalues the lives of disabled people.

Equality, fairness and inclusion for everyone in society

5.19 NIPT might impact on equality, fairness and inclusion for everyone in society in the following ways:

- **Appropriate and proportionate use of public resources:** in future, the use of NIPT for a wider range of traits and conditions, including less serious conditions and non-medical traits, might raise issues relating to the fair use of public resources, were such tests to be offered in the NHS. For example, the use of NIPT in the NHS to reveal information about fetal sex, where this has no clinical utility, might not be considered to be an effective or proportionate use of public money.
- **Changing conceptions of health:** it is possible that, if in future prenatal testing becomes more effective and women and couples are able to access even more information on

a wider range of areas about their pregnancies, views about what is considered to be a healthy pregnancy or child may gradually change.

- **Eugenics:** there are concerns about potential future uses of NIPT as a tool to screen for, and select against, specific medical conditions or impairments, or other traits. Many would view Government-funded screening programmes for less significant conditions, which might be implemented as a means of 'improving' the genetics of the wider population, as a morally problematic form of eugenics and unacceptable for that reason. It might be also viewed as in tension with trends in health and other policies that promote inclusion, equality and diversity.
- **'Designer babies':** concerns have been expressed about women and couples in the future using NIPT to select against non-medical features that they do not want their children to have in order to ensure that their offspring have certain attributes. There might be longer term negative societal consequences of the use of NIPT to further parents' aspirations for 'designer babies' which may emerge if those with the means to purchase NIPT for non-medical reasons use it in this way, whilst those with less means are not able to do so. Efforts to use NIPT to give birth to 'perfect babies' might be considered to fail to appreciate the gifted nature of children, and may also threaten the biological benefits conveyed by genetic diversity in the human species.
- **'Improving' the genetics and health of all future people:** it has been argued that reproductive technologies can be used to improve the circumstances of people of the future and minimise what some might see as natural, genetic inequalities, which sometimes correlate with wealth and other inequalities. Some think that there can be moral duties to use NIPT and reproductive technologies for these purposes and that allowing genetic variation, impairment and disability to continue to exist when we have the means to reduce these things would be wrong.

An ethical approach

- 5.20 The tensions that exist between the potential benefits of current and possible future uses of NIPT and the risks with which these uses are associated, as well as between the ethical values to which they relate, create challenges for public policy. Women and couples may experience many benefits from the enhanced reproductive autonomy that NIPT can provide as a prenatal test of superior accuracy and safety that can be performed earlier in pregnancy. On the other hand, there may be risks; for example, access to NIPT could give rise to harms to women and couples, disabled people, future people, and wider society, in terms of exacerbating or entrenching inequalities. The sum total of multiple individual free choices may add up to a harmful outcome for society as a whole. Policy makers have to align the responsibilities that the state has to support women to make informed reproductive choices about their pregnancies, with the responsibilities that it has to protect people from harm and to promote equality, inclusion and fair treatment for all. In other words, NIPT should be implemented in a way that provides improved reproductive outcomes for women while not causing harm or worsening societal inequalities.
- 5.21 Despite the tensions that exist between the values that are relevant to NIPT, the Working Group found considerable agreement amongst those with a personal or professional interest in the topic, including on the importance and relevance of these values. For example, many of those who engaged in our evidence gathering activities seemed to accept that choice, autonomy and consent, avoidance of harm, and equality, fairness and inclusion are important goods that should be respected or promoted. There appears

to be significant consensus on the importance of supporting reproductive choices but, at the same time, strong views that people should be protected from harms and efforts to promote equality, fairness and inclusion in society should not be undermined. Disagreements in this area tend to focus on the likelihood of negative consequences, or the priority each of these values should be accorded in issues of public policy.

- 5.22 It would be an over-simplification to present the ethical dimensions of NIPT as falling into two entirely distinct categories, with the benefits of NIPT associated exclusively with opportunities for enhanced choice and the drawbacks of NIPT linked with the risk of harms and negative impacts on equality, fairness and inclusion. The challenges of NIPT relate to issues of choice and autonomy as well as to the risk of harm, and challenges to equality, fairness and inclusion. For example, concerns about consent and the potential for routinisation arise from how NIPT, as a non-invasive procedure, might sometimes work to impact negatively on the prospects for women's informed choices. There are also concerns that enhanced choices for women could close down choices for their future children. Similarly, the proposed benefits of NIPT do not relate only to choice. The enhanced reproductive choices provided by NIPT are continuous with those provided by reproductive options that have helped to make our society fairer and more equal for women and are likely to support these trends, insofar as they increase the control that women are able to exert over the circumstances under which they become mothers. Making NIPT available in the NHS might address issues relating to health inequalities that might be worsened by NIPT currently being available only to those who can afford it through the private sector.
- 5.23 Importantly, most of those with whom the Working Group engaged did not seem to be advocating either completely unrestrained reproductive choice or state-enforced equality of outcomes. Many of those who took part in our evidence gathering activities and expressed views that were supportive of reproductive autonomy did not attempt to defend full reproductive choice entirely and unrestricted access to NIPT. Similarly, not all of those who expressed concerns about the potential implications of NIPT for equality and fair treatment of disabled people, for example, suggested that reproductive choices should be constrained in whatever way necessary to remove any possibility that inequalities may be worsened, and that women should therefore be prevented from accessing NIPT altogether. More commonly, those who engaged with our evidence gathering activities expressed the view that some degree of reproductive choice is good, that risks of harms should be minimised and that there should be sustained and concerted Government efforts to promote equality, fairness and inclusion, without giving rise to undue state interference.
- 5.24 With this in mind, the Working Group believes that there are ways of promoting reproductive autonomy and providing choice, whilst minimising potential harms and supporting an equal, fair and inclusive society by adopting three general principles that should always be considered together.

Principle 1. The wider societal environment in which NIPT is provided and developed should be considered when developing policy relating to NIPT

- 5.25 The Working Group believes that the state has a general duty to promote an equal and inclusive society, and that wider societal inequalities and injustices should be taken into account when developing policy, regulation and law pertaining to NIPT.

- 5.26 The wider societal and political environment can play a significant role in influencing how reproductive choices are viewed and weighed by women and couples (see Principle 2, below). Concerns about the ongoing inequality of disabled people in the UK and the genuine challenges many disabled children and adults face in accessing adequate healthcare and social support, as well as educational and employment opportunities, are likely to influence the ways in which women and couples appraise their reproductive choices. We believe that duties to support informed reproductive choice therefore extend to acknowledging responsibilities to ensure that disabled people are supported, included and valued in society. Although we recognise the gains made in securing greater rights for disabled people over the last 50 years, there should be broader efforts made by the Government and others to confront any institutional and societal biases and prejudices against disabled people and to tackle discrimination, stigma and exclusion. This includes responsibilities to shape societal attitudes and has implications for public awareness as well as medical education and training. It is our view that women and couples would be better able to make genuine choices about their pregnancies if all disabled children were actively welcomed when they are born into the world and valued as equal to those without disabilities.
- 5.27 The Working Group believes that any potential long-term impacts on disabled people and their families of the growing use of NIPT should be taken into consideration in policy making. Screening policy more generally should be sensitive to the possibilities that people with tested-for conditions and their families may become more isolated when the incidence of a condition is greatly reduced. They also may be exposed to attitudes of disapproval or blame in the event that NIPT comes to be seen as a standard part of pregnancy care. The language of screening must be respectful to all those concerned, particularly women and disabled people.
- 5.28 The Working Group has concerns about the potential future uses of NIPT for less significant medical conditions and impairments, non-medical traits and whole genome and exome sequencing that relate to the potential long-term societal implications of such uses. If NIPT technology develops in this way, it is possible that information from prenatal tests could be used to inform decisions about terminating pregnancies on a much broader range of grounds than is possible with current prenatal testing technologies. The Working Group is concerned about the potential that NIPT has to impact on women and couples' expectations of their future children, on what is considered to be a healthy pregnancy, and on the diversity and inclusion of difference in society more generally.

Principle 2. Pregnant women and couples should have access, where appropriate, to NIPT within an environment that enables them to make autonomous, informed choices

- 5.29 The Working Group takes the view that pregnant women should have access to NIPT, but only within an environment that enables them to make autonomous, informed reproductive choices about their pregnancies.
- 5.30 We believe that supporting reproductive autonomy involves proactive duties to ensure that women are in a position to make informed decisions to undergo NIPT. For example, NIPT must provide accurate and reliable information about the genetic condition or impairment that the fetus is being tested for. In addition, the fact that NIPT, and prenatal screening more generally, is optional must be emphasised when it is offered to women and couples in the NHS; NIPT should not be presented as a routine part of antenatal care. It also should be made clear to women and couples that there are no expectations about what is the 'right' decision about undergoing NIPT, about undergoing further

prenatal testing following NIPT, or about whether to subsequently continue with or terminate a pregnancy following a diagnosis.

- 5.31 It is important that accurate, balanced and non-directive information is made available to women and couples in both the private and public sectors so that they can make informed decisions about whether or not to undergo NIPT. This information should include not only clinical information, but also information about the lived experience of disability i.e. what it is like both to have, and to look after a daughter or son with a condition for which NIPT can test for in a fetus. The same levels of high quality care and support must be provided to women who choose to have further tests and those who choose no further tests. Similarly, high quality care must be equally provided to women who proceed with pregnancies that are affected by genetic variation and to women who choose to terminate the pregnancy.
- 5.32 The Working Group believes that enabling women to exercise reproductive autonomy involves cultivating a wider societal environment in which voluntary, informed choices about continuing or terminating a pregnancy that is affected by genetic variation are possible, free from duress. In order for women to be in a position to make such decisions about their pregnancies, the context in which they make these choices must be as free as possible from external pressures. These pressures may come from personal, commercial, institutional and societal influences, biases and prejudices. Where these exist, we believe that they must be confronted and addressed. In further support of Principle 1, women and couples must also feel confident that they would receive appropriate levels of care and support as parents of a disabled child in the UK.

Principle 3. Efforts should be made to reduce any risks of significant harms posed by the growing use and development of NIPT

- 5.33 The Working Group believes that, whilst women should have access to NIPT, action should be taken to minimise the risks of significant harm where such risks exist. In order to achieve this, in some cases it may be appropriate for the provision of NIPT to be adapted, controlled or restricted. This might be necessary if there are, for example, uncertainties about the safety, accuracy, clinical utility or responsible promotion of NIPT.
- 5.34 For example, the possibility that delays in fetal diagnoses of Down's, Edwards' and Patau's syndromes will follow the introduction of NIPT as a second stage screening test in the NHS may give rise to increased anxiety for some women and couples. This, in addition to the potential harms to women and fetuses associated with later terminations, should be taken into account when deciding how to integrate NIPT within an NHS care pathway and support women who choose to have NIPT.
- 5.35 Providers should not mislead women and couples about the limitations of NIPT, nor exploit or exacerbate anxieties about their pregnancies. They should give women and couples sufficient time to consider whether they want to undergo NIPT or not, and each decision accepted as equally valid. All providers of NIPT have a responsibility to ensure that women and couples are well supported before and after undergoing NIPT.
- 5.36 The availability of NIPT where the accuracy of the test is poor or unknown may give rise to unnecessary anxiety in women and couples and may increase the number of women seeking invasive diagnostic procedures following NIPT. This could increase the number of procedure-related miscarriages, posing harms to women, couples and fetuses. Both public and private sector providers of NIPT must take account of the potential harms

connected with possible unanticipated or secondary findings about the mother's health or inconclusive results in the ways in which they offer, explain and discuss NIPT.

- 5.37 The Working Group is mindful of the possible harms of extending the use of NIPT beyond testing fetuses for information that could have a direct bearing on the immediate or early health of fetuses and future children. This includes future uses of NIPT to test for a range of genetic traits, including adult onset conditions where this is 'for information only', carrier status, less significant medical conditions and impairments, and non-medical traits. Whole genome or exome sequencing of fetuses using NIPT may also become possible in the future, which would elicit information of this sort, as well as a large amount of information of unknown significance. These possibilities raise serious concerns about the autonomy, privacy, rights and other interests of future children and people, who should be able to make their own choices regarding information about their genetic makeup, to access the same opportunities and services as those who know nothing about their genetic makeup, and to live a life in which their future is open.

Chapter 6

Conclusions and
recommendations

Chapter 6 – Conclusions and recommendations

Chapter overview

Overarching conclusions and recommendations

Women and couples should be able to access non-invasive prenatal testing (NIPT) to enable them to find out whether their fetus has a significant medical condition or impairment that manifests at birth or in childhood. However, NIPT should only be offered if it provides an accurate prediction of whether the fetus has or does not have the condition being tested for. In addition, all providers of NIPT have a responsibility to provide high quality information and support to women and couples about the test and the condition being tested for. The Government should ensure that it is meeting its duties to provide disabled people with high quality specialist health and social care, and to tackle the discrimination, exclusion and negative societal attitudes experienced by disabled people.

NIPT should not normally be used to test whether a fetus has a less significant medical condition or impairment or an adult onset condition; to find out whether the fetus is the carrier of a gene for any kind of medical condition or impairment; nor to reveal non-medical traits of the fetus, including sex. The use of NIPT for whole genome or exome sequencing of fetuses should not normally be offered outside of a research environment.

Professional guidance for health and social care professionals on the availability and provision of all types of NIPT in the UK should be developed, and existing guidance on the continuation of pregnancy after a diagnosis of fetal anomaly should be updated and expanded.

NIPT in NHS screening for Down's, Edwards' and Patau's syndromes

We support the introduction of NIPT for Down's, Edwards' and Patau's syndromes as a second stage screening test in the NHS. Accurate, balanced and non-directive information for women and couples should be developed and published with the involvement of people with different personal experiences. High quality education and training must be compulsory for all health and social care professionals involved in NHS prenatal screening.

The UK National Screening Committee should take better consideration of the particular consequences, some of which will be unintended, of prenatal screening programmes where termination of pregnancy is an option.

NIPT for rare genetic diseases in the NHS

The NHS should ensure it has an adequate supply of trained genetic counsellors.

The use of whole genome or exome sequencing may be justified in rare cases in this context, such as when it is suspected that a fetus has a significant medical condition or an impairment of unknown origin.

NIPT in the private sector

The Committee of Advertising Practice should more closely monitor the marketing activities of NIPT manufacturers and private hospitals and clinics to ensure that they are not misleading or harmful. Certification from recognised information quality schemes should be sought by NIPT providers to help women and couples to know that their information has been quality checked. Private hospitals and clinics should only offer NIPT as part of an inclusive package of care that should include, at a minimum, pre- and post-test counselling and follow-up invasive diagnostic testing if required.

Introduction

- 6.1 The discovery that placental cell-free DNA in maternal blood can be used to obtain accurate genetic information about the fetus without presenting a risk of miscarriage represents a major breakthrough in prenatal screening and testing. The technology is already being used or will soon be used in the NHS and in the private sector to test for or estimate the likelihood of a number of genetic conditions, and this use is set to expand. Affordable and accurate whole genome sequencing of fetuses using non-invasive prenatal testing (NIPT) may be possible in the future. The main limits to the potential applications of NIPT are likely to involve the interpretation of the genetic information that it generates and the fact that the cfDNA originates from the placenta.
- 6.2 Like many new genetic technologies, NIPT raises significant ethical issues. We have explored the ways that these issues can be understood in terms of the values of choice, autonomy and consent; avoidance of harm; and equality, fairness and inclusion. NIPT offers benefits and drawbacks within each of these categories. The challenge for public policy makers will be to ensure that the benefits of NIPT are maximised while the potential harms, to individuals and wider society, are minimised. The ethical approach advocated by the Working Group is proposed as a framework for policy development pertaining to NIPT both now and in the future as the technology develops.
- 6.3 NIPT for Down's, Edwards' and Patau's syndromes will soon be introduced in the NHS prenatal screening programme; NIPT is used in the NHS to test fetuses for some significant medical conditions or impairments when there is a family history or other indication; and NIPT for these conditions and more is available through private companies. Yet, to date, there has been little consideration by public and professional bodies of the ethical issues raised by these uses of NIPT. In this chapter, the Working Group uses its ethical approach as the basis for making a number of recommendations for the ethical provision of NIPT. Many of these apply to any provider of NIPT, be they the NHS or a private company, and could apply to the use of NIPT in any country. Some specific issues are raised by the offer of NIPT as part of an NHS screening programme or other NHS service, as well as by the offer of NIPT by private healthcare providers in the UK, and some additional recommendations are made in each of these areas.

Overarching conclusions and recommendations

NIPT for significant medical conditions and impairments

- 6.4 Our ethical approach leads us to the conclusion that **women and couples should be able to access NIPT to enable them to find out at an early stage of pregnancy, if they wish, whether their fetus has a significant medical condition or impairment that manifests in childhood.** This can be helpful in informing decisions about different options for clinical interventions during pregnancy, where these are available, and preparing psychologically and practically for the birth of a disabled child. The information provided by NIPT can also help women and couples make decisions about whether to terminate a pregnancy if they wish to avoid having a child with a significant medical condition or impairment. Such conditions and impairments can have a significant effect on people's lives and opportunities, and on the lives and opportunities of their family members. This is often exacerbated by the wider social and cultural context, but the intrinsic characteristics of the condition or impairment can, in and of themselves, have significant effects on family life.

- 6.5 However, we believe that NIPT for significant medical conditions or impairments should only be available within an environment that enables, as far as possible, women and couples to make autonomous, informed choices, and when steps are taken to minimise the potential harms of offering NIPT. This, we suggest, involves the following.
- 6.6 First, **an NIPT test should only be offered if it provides an accurate prediction of whether the fetus has or does not have the significant medical condition or impairment being tested for.** Tests that do not offer this could undermine the ability of women and couples to make informed reproductive choices and might lead more women to have invasive diagnostic procedures. Such tests also would have reduced clinical utility and would constitute the provision of a poor or unacceptable healthcare service. Ideally, NIPT would be diagnostic, and this is the case when NIPT is used for some single gene disorders, such as cystic fibrosis or achondroplasia, in some circumstances. For other conditions and impairments, NIPT provides an estimate of the chance that the fetus has the conditions. In these cases, it is not straightforward to define what would constitute an accurate test. The acceptable thresholds of the different components of test accuracy (i.e. sensitivity, specificity, positive predictive value and negative predictive value) are likely to be different for each condition being tested for. Thresholds on test performance are imposed when NIPT is used within the NHS. The UK Genetic Testing Network (UKGTN), for example, evaluates the scientific validity of new genetic tests that its member laboratories would like to offer patients through NHS genetics centres (although it is possible for NHS genetics centres to access tests that have not been approved by the UKGTN). The UK National Screening Committee (UKNSC) evaluates test performance when considering whether a test should be offered as a national screening programme.
- 6.7 In the private sector, few restrictions exist, although this may change for NIPT manufacturers operating in the EU when the new EU In-Vitro Diagnostic Medical Devices (IVD) Regulation comes into force in 2017 (see Paragraph 4.5). This has led to the offer of NIPT for some conditions, including those caused by certain microdeletions, where the test has not been shown to provide an accurate prediction of whether the fetus has or does not have the condition being tested for. Until evidence of good test performance and scientific consensus on what is good performance in each case is available, we recommend that healthcare professionals working in the private sector in the UK should stop offering any such tests. Professional regulators and regulatory bodies such as the General Medical Council and Nursing and Midwifery Council, the Care Quality Commission, and regulatory bodies in Scotland, Wales and Northern Ireland, should ensure that the healthcare providers and activities that they regulate are only offering NIPT tests that are known to be accurate to a level that is appropriate to the condition or impairment being tested for. In addition, **NIPT should be included in the 'regulated activities' that are regulated by the Care Quality Commission, to ensure that the provision of NIPT by hospitals and clinics in England is carried out to high standards of quality and safety, even when NIPT is accessed by pregnant women and couples on a one-off basis.**
- 6.8 Secondly, **providers of NIPT for significant medical conditions or impairments should ensure, through the provision of high quality information and support, that the following is understood by women and couples as part of the offer of testing:** the optional nature of testing; the meaning and implications of a positive or a negative test result; the benefits and limitations of the test (particularly positive predictive values); the choices that testing may lead to; the possibilities of test failure and of unanticipated or secondary findings about the mother; and what they might expect from life with a child or adult with the condition being tested for. We believe that NIPT for significant medical conditions or impairments should always be offered in healthcare settings by skilled

healthcare professionals to ensure that the appropriate information and support is available. The type and level of knowledge required of professionals in order that they can support women and couples to make informed choices, and the time required to deliver that support to a high standard, will vary at different stages of the pathway. Professionals involved in counselling women and couples before testing should have good knowledge of NIPT, its benefits and limitations, the conditions being tested for, invasive testing and all options following a diagnosis. Professionals involved in delivering NIPT results should deliver a diagnosis or high chance result in an appropriate way, recognising the anxiety this may cause but ensuring that the implications of results are understood. Women and couples with a positive diagnosis or a high chance result should have timely access to the information and support they require. Professionals involved in supporting women and couples to make choices at this stage should have access to high quality information on what it is like to have a child or adult with the condition or disability in question and how this can vary for different individuals and families. They should understand the specificity, sensitivity and positive and negative predictive values of NIPT for different women and different conditions and, if NIPT is not diagnostic, they should understand the risks associated with invasive diagnostic testing. They should be knowledgeable about the implications of a choice to continue or terminate a pregnancy and the different methods of termination that are available. Such knowledge is likely to require the involvement of professionals from a range of specialities, such as obstetricians, paediatricians, paediatric surgeons, geneticists, neonatologists, registered learning disability nurses, special needs teachers, social workers, and others with first-hand knowledge of children and adults with the condition or disability and their families.

- 6.9 Similarly, the required information should be readily available to women and couples in written or multimedia formats. Again, such information should be accurate, balanced in presentation, and non-directive, and should be developed jointly by professionals and others with a range of expertise and experience, including people with genetic conditions and their families. Worked examples of what different test results mean for different women may be helpful; for example, if a high chance test result has been received, how likely it is that the fetus will have the condition or impairment. The fact that difficult choices about continuing or terminating a pregnancy may need to be made as a result of having NIPT should be raised.
- 6.10 Access to independent sources of information and support i.e. from those not involved in the delivery of NIPT, is also important for enabling women and couples to make informed choices related to NIPT. As the only prenatal testing support organisation to which the NHS directs pregnant women, it is important that Antenatal Results and Choices provides balanced, non-directive and impartial advice to parents, and balanced information via training to health professionals. While there is no evidence that they are not meeting these aims, we recommend that they work with more people with experience of continuing a pregnancy after a diagnosis of fetal anomaly in the delivery of their services.
- 6.11 Thirdly, **the Government should ensure that it is meeting its duties to provide disabled people with high quality specialist health and social care and to tackle discrimination, exclusion and negative societal attitudes experienced by disabled people.** This is important for offsetting the potential harms posed by the use of NIPT for significant medical conditions or impairments to disabled people and their families. This is also important given our view that women and couples will be better able to make genuine choices about their pregnancies if all disabled children are actively welcomed when they are born and valued as equal to those without disabilities. A collective effort

should be made to better acknowledge the lived experience of disability and to challenge the view that caring for a disabled child is necessarily burdensome or undesirable. Organisations and individuals that are subject to the Public Sector Equality Duty, such as health and social care providers, the BBC, providers of medical education and training, and schools and other education providers, have a particular duty to tackle the discrimination and exclusion experienced by disabled people.³⁷²

NIPT for other conditions and traits

- 6.12 Looking to the future, NIPT opens up possibilities for testing fetuses for a much wider range of genetic conditions and traits than is currently possible at an early stage of pregnancy and without posing a risk of miscarriage. These might include less significant medical conditions and impairments, adult onset conditions, carrier status for genetic conditions and non-medical traits. NIPT for one non-medical trait, sex, is already widely available. Using NIPT to carry out whole genome or exome sequencing, which could reveal information of all these types and more, is also a likely prospect. It is important for policy makers to be prepared and to consider the potential consequences of such eventualities before they become available. Although we support the principle that women and couples should have access to NIPT within an environment that enables them to make autonomous, informed choices, we also believe that efforts should be made to reduce any risks of significant harms posed by the use of NIPT, including the potential impacts on the wider societal environment, when developing policy and regulation relating to NIPT. If the potential harms are significant enough, the Working Group believes that there are limits to the kinds of reproductive choice that NIPT should be used to facilitate. However, in many areas there is a lack of evidence relating to the risk of harms, what those harms might be and the extent of those harms. Our conclusions will need revisiting in the event of any new evidence that comes to light.
- 6.13 After weighing up the potential benefits and harms, **we believe that NIPT normally should not be used to test whether a fetus has a less significant medical condition or impairment or an adult onset condition; to find out whether the fetus is the carrier of a gene for any kind of medical condition or impairment; nor to reveal non-medical traits of the fetus.** Using NIPT in this way would provide pregnant women and couples with information to which they might feel they have a right, and it might help them prepare psychologically and practically for the birth of a baby with a condition or trait. However, some women who obtain information of this kind so early in pregnancy may be motivated to seek further tests or terminations, which could have a range of harmful consequences (see Paragraphs 3.33-3.36 and 4.51-4.59). In addition, accessing this kind of information could, in some circumstances, undermine the capability of the future person to make their own choices about accessing their genetic information and close down some of their future life options. A further concern is that, given that such information usually would not be grounds for termination and would have no clinical use prenatally, offering such tests could be regarded as not meeting the responsibilities of health and social professionals to ensure that all patients receive good care and treatment. We suggest that, in line with professional guidance on the genetic testing of children, use of NIPT that is primarily predictive of future impairment or reproductive risks in the fetus, as opposed to informing decisions about immediate medical care, should normally be delayed until the future person can decide for him/herself when, or whether, to be tested. It is already possible to access NIPT in the private sector for some conditions that might not be generally considered to be significant medical conditions or

³⁷² Guidance on meeting the requirements of the Public Sector Equality Duty is available at: <https://www.equalityhumanrights.com/en/advice-and-guidance/public-sector-equality-duty>.

impairments, such as triple X syndrome. We recommend that private providers stop offering any such tests for the reasons outlined above.

- 6.14 It is possible to imagine several exceptions to our recommendation, however. For example, **an exception might be posed by woman and couples with a family history of an adult onset condition who want to find out if their fetus will develop the condition, if the condition is extremely serious and manifests in mid-life, if there is no treatment available, and if termination of pregnancy is an option.** Prenatal testing for Huntington's disease is already available to families with a history of this condition using invasive testing methods if they wish to have it, and it could be acceptable to use NIPT to test for this very serious condition as well. Testing for conditions such as this should always be accompanied by high quality counselling with genetics professionals to enable parents to consider the consequences of testing, particularly if they decide to continue with the pregnancy.
- 6.15 A further exception might be posed by the use of NIPT for determining the sex of a fetus, which is already widely available in the UK through private companies. Finding out the sex of the fetus may not, in and of itself, undermine the rights of the future child or have the potential to harm the development of the future child, given that the sex of the future child will usually be revealed at birth or, very often, on a fetal ultrasound scan. This might also be true for other non-medical traits that manifest in physical features that are apparent at birth. The ability of NIPT to reveal the sex of the fetus at a much earlier stage does, however, increase the risk of terminations on the basis of sex taking place. The Working Group believes that sex selective terminations will almost always be based solely on sexist and discriminatory attitudes. There is some evidence that sex selective terminations have taken place in the past in the UK, although it is not clear, if this were to continue, whether this would be likely to cause a general population imbalance in the UK. However, sex selection is considered to be a serious issue in South and East Asia and in population subgroups drawn from those regions who reside in other countries, such as the USA. There is a real possibility that the same practices may be encouraged within the UK, either among UK residents who originate from those areas or through 'sex selection tourism', by the availability of NIPT for sex determination. Permitting the early disclosure of fetal sex in the UK could undermine efforts being made internationally to tackle these problems, and the Working Group believes that the UK should support the efforts of these countries – and campaigners for the rights of women more generally – to confront and prevent this form of sex discrimination.
- 6.16 In conclusion, the consequences of an increase in sex selective terminations in the UK are potentially serious, particularly within specific cultural communities, and the medical benefits to a pregnant woman of finding out the sex of her fetus at nine to ten weeks, rather than at later ultrasound scans, are few. **Therefore, we recommend that NIPT providers should not offer sex determination of fetuses. We believe that the Government should require test providers to neither generate nor report this information unless there is concern that the fetus may be showing signs of a significant sex chromosome aneuploidy or is at risk of a sex-linked disorder. This should apply to providers and manufacturers whose products are used by women in the UK, wherever the laboratory analysis takes place.**
- 6.17 As it becomes possible to test for more conditions and traits using NIPT in the future, further exceptions may arise to our recommendation that NIPT should not be normally used for less significant medical conditions or impairments, adult onset conditions, carrier status or non-medical traits. **We recommend that before any new tests that reveal**

information of this sort are offered, the implications in terms of choice, consent and autonomy, the potential harms, and the wider consequences for society are taken into account.

NIPT for whole genome and exome sequencing

- 6.18 It is possible that whole genome and exome sequencing of fetuses using NIPT will be available within NHS genetic testing services and in the private sector in the near future. Potentially, the pregnant woman or couple would have access to any interpretable genetic information about the fetus, as well as a large amount of information of unknown significance. We have already set out the reasons why we believe NIPT normally should not be used to reveal information about a fetus relating to less significant medical conditions or impairments, adult onset conditions, carrier status, sex or other non-medical traits, and why whole genome or exome sequencing normally should not be offered. Any restrictions on access to information about the fetus would also need to apply to whole genome or exome sequencing, otherwise these restrictions could be bypassed. Additional concerns are raised by the prospect of whole genome or exome sequences of fetuses being generated and stored, potentially enabling information that was uninterpretable at the time to be analysed and interpreted in the future when genetics research has advanced. In rare circumstances, the use of whole genome or exome sequencing may be justified, such as when it is suspected that the fetus has a significant medical condition of unknown origin. However, in line with international professional guidelines on prenatal testing, targeted testing should be used in most cases, and if whole genome or exome sequencing is used, comprehensive patient counselling from qualified health and social care professionals will be essential. **However, the Working Group strongly recommends that the use of NIPT for whole genome or exome sequencing of fetuses normally should not be offered outside of a research environment governed by a research ethics framework**, apart from in some exceptional cases (see Paragraph 6.37). **We recommend that the Government considers establishing a moratorium with NIPT manufacturers to agree that prenatal whole genome or exome sequencing will not be offered to pregnant women and couples in the UK for the foreseeable future.**

Professional guidance

- 6.19 There is no UK-specific professional guidance on NIPT. **We recommend that professional guidance for health and social care professionals on the availability and provision of NIPT in the UK should be developed by relevant Royal Colleges, the Joint Committee on Genomics in Medicine, and other professional bodies.** The guidance should cover the use of NIPT for screening and testing, for different conditions and traits and for whole genome and exome sequencing. The guidance should be aimed at all health and social care professionals involved in prenatal genetic screening and testing both in the NHS and the private sector, and should highlight the obligations of staff to meet standards of care set by professional regulators such as the General Medical Council and the Nursing and Midwifery Council. The guidance should set out the responsibilities of health and social care professionals to provide tests that are known to be accurate to a level that is appropriate to the condition or impairment being tested for. It should cover the provision of accurate, balanced and non-directive information and support, result giving, dealing with unanticipated or secondary findings and failed tests, and issues related to conscientious objection. The guidance should recognise the differences between the four countries of the UK in terms of the law on abortion and the health and social care that is available to NHS patients.

- 6.20 In addition, **the Royal College of Obstetricians and Gynaecologists guidance for its members on the termination of pregnancy for fetal anomaly should be renamed immediately to indicate that they cover the continuation of pregnancy after a diagnosis of fetal anomaly, and this part of the guidance should be expanded significantly, or additional guidelines created.** The guidance should be updated to include the care of women who receive a high chance or positive NIPT result as well as those who undergo invasive diagnostic testing. It should be emphasised that following a diagnosis or a high chance NIPT result, women should have access to advice from a wide range of experts, including those with first-hand knowledge of children and adults with genetic conditions and impairments and their families, and they should have the option of receiving specialist care and support throughout their pregnancy or remaining on the standard antenatal care pathway. In addition, the **National Institute for Health and Care Excellence (NICE) should produce clinical pathway guidance on the continuation of pregnancy after diagnosis of fetal anomaly.**

Specific conclusions and recommendations

- 6.21 The recommendations made so far apply to all kinds of uses of NIPT in the NHS and private sector. In this section we make some additional conclusions and recommendations for specific uses of NIPT based on our ethical approach of promoting reproductive autonomy and choice, whilst minimising potential harms and supporting an equal and fair society.

NIPT in NHS screening for Down's, Edwards' and Patau's syndromes

- 6.22 We did not consider in this report whether prenatal screening for Down's, Edwards' and Patau's syndromes specifically should be offered in the NHS. However, **we do not support the view that prenatal screening for Down's, Edwards' and Patau's syndrome is intrinsically wrong.** To attempt to mitigate the hurtful or offensive messages, or other harmful effects that screening might have for people with Down's, Edwards' or Patau's syndromes, concerted and sustained efforts should be made to show that society values people with these syndromes, and other genetic conditions and variations, and to ensure that they are provided with comparable opportunities for a good life as those without such a condition (see earlier recommendation, Paragraph 6.11). In the case of Edwards' and Patau's syndromes, this includes the offer of active treatment as well as palliative care only.
- 6.23 Offering NIPT as a second stage test for Down's, Edwards' and Patau's syndromes as part of the NHS prenatal screening programme has the potential to enable choice by giving women the opportunity to prepare for a disabled child or to have a termination (in countries where this is available). However, there are concerns that it could undermine informed choice if NIPT becomes a routine or expected procedure, or if the information and support women receive is incomplete, out-of-date or perceived as being directive in any way. Offering NIPT will reduce harms by lowering the number of invasive diagnostic tests that are carried out, therefore reducing the number of procedure-related miscarriages, and it may lead to the avoidance of some late terminations. However, there is a risk that it may increase harms if it is taken by women to be equivalent to a diagnostic test, if it delays diagnosis for some women (delaying some terminations) and if it makes life more difficult for people with the conditions being screened for. Offering NIPT on the NHS may promote equality and fairness in society by giving women equal access to the test and providing them with more choice over the circumstances of parenthood. On the

other hand, there are concerns that offering NIPT could undermine equality and fairness by increasing discrimination and devaluing the lives of disabled people.

- 6.24 **The Working Group supports the introduction of NIPT for Down's, Edwards' and Patau's syndromes in the NHS for women who have been found to have at least a 1 in 150 chance of having a fetus with one of these conditions.** Given the uncertainties surrounding the implications of introducing NIPT, the lower positive predictive value of NIPT when used in the general population of pregnant women, the significant failure rate of NIPT, and the substantially higher costs of offering NIPT to all women, we believe offering it to women only in the higher chance category within an evaluative roll-out is a proportionate and ethical approach at the current time.
- 6.25 **The relevant parts of the professional guidance recommended above (see Paragraph 6.19) should be incorporated into existing NICE guidance, NHS service specifications and other relevant NHS guidance across the UK.** This should cover all stages of the pathway and include the provision of accurate, balanced and non-directive information and support, result giving, and dealing with any unanticipated or secondary findings and failed tests.
- 6.26 **High quality education and training must be compulsory for all health and social care professionals involved in the delivery of NIPT within the NHS prenatal screening pathway.** Training should have agreed learning outcomes that cover: the provision of accurate, balanced and non-directive information about the tests and conditions tested for; skills in providing decision-making support and the need for reasonable adjustments to support decision making for those with protected characteristics; and knowledge about the medical and social prospects of people with the conditions being screened for. The training would be enhanced by the involvement of people with different personal experiences of prenatal screening and the conditions being screened for. It is recommended that Public Health England and the fetal anomaly screening programme work with support organisations to deliver these different aspects of training and that this continues as part of a sustainable fetal anomaly screening training programme going forward.
- 6.27 **Public Health England, relevant bodies in other UK countries and the NHS Choices website should develop and publish accurate, balanced and non-directive information for women and couples on NIPT and other prenatal screening tests.** This should be available in a variety of formats to take account of the different people who might read it, and include information on the benefits and limitations of NIPT and other screening and diagnostic tests (particularly their positive predictive values), what parents might expect from life with a son or daughter with the conditions being screened for, and the options available to women who receive a high chance result or diagnosis, including the care and treatment that they might expect to receive in each case. Again, the information would be enhanced by the involvement of people with different personal experiences of prenatal screening and the conditions being screened for. **The lack of information on continuation of pregnancy after the diagnosis of a fetal anomaly on the NHS Choices website should be rectified as soon as possible. In addition, Public Health England and the fetal anomaly screening programme should provide detailed briefings for journalists when NIPT is introduced to help ensure that accurate information about NIPT and the conditions being tested for is reported in the media.**
- 6.28 The introduction of NIPT as a second stage test is likely to increase both the number of points at which information needs to be provided and, to some degree, the amount of information to be provided and discussed. It may be helpful to set out the points in the

screening pathway at which pregnant women and couples should be receiving information and support from the NHS to enable them to make informed decisions about screening. Different information resources, in terms of the detail and content of the information, may need to be developed for different points in the pathway and depending on the different conditions being screening for. Based on the professional guidance that exists on the provision of information and support, the new 'information pathway' might be summarised as follows:

- i. **Initial contact** – during the first encounter with a healthcare professional, pregnant women should receive written information about the optional nature of screening, the conditions that can be tested for, the accuracy and practicalities of the combined test, and the options available in the event of a high chance result. A skilled health or social care professional should also provide this information verbally and in such a way as to equally support decisions to test and not to test. Women will be asked to decide at this point if they want to have the combined test.
 - ii. **Combined test results** – women who opt for the combined test and receive a low chance result should be informed of this in an appropriate way and informed that no further testing will be offered. Women who receive a high chance result from the combined test should be informed in an appropriate way and be given rapid opportunity to discuss the result with skilled health or social care professionals. Information should be provided in a non-directive way about the implications of the result, the condition(s) for which the high chance result is for, and the options available (i.e. no further testing, NIPT or a diagnostic test). A skilled healthcare professional should provide this information verbally and in such a way as to equally support decisions to test or not to test.
 - iii. **NIPT results** – women who opt for NIPT and receive a low chance result should be informed in an appropriate way and informed that no further testing will be offered. Women who receive a high chance result should be informed in an appropriate way and given rapid opportunity to discuss the result with skilled health or social care professionals. Information should be provided in a non-directive way about the implications of the result, the condition that has been identified as likely, and the options available (i.e. no further testing or a diagnostic test). A skilled healthcare professional should provide this information verbally and in such a way as to equally support decisions to test or not to test.
 - iv. **Diagnostic testing results** – women who opt for diagnostic testing and receive a negative result should be informed in an appropriate way and informed that no further testing will be offered. Women who receive a positive result should be informed in an appropriate way and given rapid opportunity to discuss the result with skilled health or social care professionals. Information should be provided in a non-directive way about the implications of the result, the condition that has been detected, and the options available (i.e. continuation or termination of the pregnancy). A skilled healthcare professional should provide this information verbally and in such a way as to equally support decisions to terminate and to continue the pregnancy.
- 6.29 Given the possibility that offering NIPT as a second stage screening test may lead to a delay in diagnosis for some women, **we support the proposal of the Fetal Anomaly Screening Programme to offer women the option to proceed directly to invasive diagnostic testing after a high chance combined test result if they wish.**

- 6.30 Before NIPT is offered to women in the NHS prenatal screening programme, **the NHS will need to ensure that it can respond to any changes in demand for related services such as genetic counselling, invasive diagnostic testing, termination and laboratory services.**
- 6.31 **An evaluation of the introduction of NIPT for Down's, Edwards' and Patau's syndromes in the NHS will be important for considering whether and how NIPT will be offered in the future.** An evaluation should include: the experiences of people who are offered NIPT, how this offer was made and the pre- and post-test counselling received; any effects on the decisions pregnant women in the UK are making in relation to whether to have screening or not, and whether to continue or terminate a pregnancy following a high chance result or diagnosis; the period in gestation at which women are receiving diagnoses; the rate of failed and inconclusive results, and unanticipated or secondary findings about the woman; and the impact of the introduction of NIPT on linked NHS services, such as genetic counselling, diagnostic testing, termination and laboratory services.

Future decisions regarding NHS prenatal screening

- 6.32 It is possible that NIPT for additional genetic conditions, or whole 'panels' of genetic conditions, will become candidates for future prenatal screening programmes that will need assessment by the UKNSC in the future.³⁷³ There have been recent calls on governments and public health authorities to adopt an active role in ensuring the responsible introduction of prenatal screening on the basis of ethical principles, especially where prenatal screening is offered as part of a public health programme.³⁷⁴ We believe that an examination of the aims of and criteria for NHS prenatal screening programmes, where termination of pregnancy is an option, to be timely.
- 6.33 **We recommend that the UKNSC takes better consideration of the particular psychological, ethical and social consequences, some of which will be unintended, of any prenatal screening programme where termination of pregnancy is an option.** For example, in relation to NIPT, it is important to consider anxiety for women undergoing NIPT and receiving a high chance result, the impact of false positive NIPT results on women who have diagnostic testing or who continue a pregnancy with no further test, and the impact on those who choose to terminate or continue their pregnancy following a diagnosis of fetal anomaly. There is limited evidence on the psychological consequences on women of having NIPT. In addition, consideration should be given to the social consequences related to any reduction in the number of people with the conditions being screened for; and the potential for sending hurtful or damaging messages to people with the condition and their families. In particular, we recommend that the UKNSC:
- develops specific criteria for assessing the viability, effectiveness and appropriateness of prenatal screening programmes where termination of pregnancy is an option that take into consideration the different issues raised, as compared to adult screening programmes;

³⁷³ Boardman FK, Young PJ and Griffiths FE (2017) Population screening for spinal muscular atrophy: A mixed methods study of the views of affected families *American Journal of Medical Genetics Part A*: 421-34

³⁷⁴ Dondorp W, de Wert G, Bombard Y *et al.* (2015) Non-invasive prenatal testing for aneuploidy and beyond: challenges of responsible innovation in prenatal screening *European Journal of Human Genetics* **23**: 1438-50

- ensures these criteria recognise and consider the wider potential consequences of screening on different parties in appraisals of existing and new prenatal screening programmes;
- develops a better understanding, through research, of the factors that influence the extent to which pregnant women are making informed decisions, in order to help ensure women have access to the information and support they need to make informed decisions, whatever they may be;
- improves the way it considers the ethical and social issues raised by prenatal screening, and the transparency of its processes, as recommended in the 2015 review of the UKNSC.³⁷⁵ This might involve, for example, improved public engagement activities, stronger relationships with organisations representing stakeholders, better representation of experts on ethics and social science on the UKNSC, and commissioned reviews of ethical literature and empirical data on the impacts of screening on different groups. The outcomes of such activities and how they have been taken into consideration by the UKNSC should be publicly available.

NIPT for rare genetic diseases in the NHS

- 6.34 NIPT can enable women who have a rare genetic condition, a family history of a condition, or who have had a fetal anomaly detected on an ultrasound scan, to make informed choices about their pregnancy. It can provide early, diagnostic information about significant medical conditions or impairments without putting the fetus at risk, giving women the opportunity to prepare psychologically and practically for a disabled child, or to have a termination. This kind of NIPT is usually accompanied by the provision of pre- and post-test information and support by a team of specialist health and social care professionals.
- 6.35 The UK Genetic Testing Network (UKGTN) evaluates the scientific validity and clinical utility of new genetic tests that its member laboratories would like to offer NHS patients according to stringent criteria. Genetics centres can access genetic tests that are not approved by the UKGTN, including tests offered by non-NHS laboratories and those based outside of the UK. However, the offer of any prenatal genetic test to NHS patients usually involves genetics professionals, such as clinical geneticists, who decide what tests should be offered and to which patient. Given this, we do not believe that further regulation of prenatal genetic testing taking place within the NHS, including NIPT, would be warranted. However, **UK-specific guidance for health and social care professionals involved in the provision of NIPT for rare genetic conditions to NHS patients would be helpful, and the scope of the professional guidance recommended above should include this kind of offer and use of NIPT** (see Paragraph 6.19).
- 6.36 To ensure NHS patients receive the information and support they need to make decisions relating to NIPT for rare genetic conditions, and to meet the potential rise in demand for prenatal diagnosis brought about by the increasing availability of NIPT for

³⁷⁵ UK National Screening Committee (2015) *Review of the UK National Screening Committee (UK NSC)*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/443953/20150602_-_Final_Recommendations.pdf.

rare genetic conditions, **the NHS should ensure that it has sufficient genetic counselling resources.**

- 6.37 To reiterate our recommendation above, **the use of whole genome or exome sequencing may be justified in rare cases, such as when it is suspected that a fetus has a significant medical condition or impairment of unknown origin.** Professionals working in NHS genetics centres are most likely to find themselves confronted by this kind of situation. In line with international professional guidelines on prenatal testing,³⁷⁶ targeted testing should be used in most cases, and if whole genome or exome sequencing is used, comprehensive patient counselling from qualified health and social care professionals will be essential.

NIPT in the private sector

- 6.38 The availability of NIPT for significant medical conditions or impairments in the private sector can provide women and couples, who have the financial means, with information about their fetus at an early stage of pregnancy and without undergoing combined screening. This information can then inform decisions about further testing. The availability of NIPT in the private sector to those women and couples who do not qualify for NIPT in the NHS therefore increases access to NIPT, albeit only for those with the financial means.
- 6.39 The ability of women and couples to make informed choices may be hampered if there is a lack of accurate, balanced, non-directive information about the test and the condition being tested for. Some NIPT manufacturers, private hospitals and clinics, and healthcare professionals working in the private sector are not meeting their obligations to provide high quality information and support to pregnant women. **We reiterate our earlier recommendation that all NIPT providers, including manufacturers and private hospitals and clinics, should provide accurate, balanced and up-to-date information for pregnant women and couples about the benefits and limitations of NIPT and the conditions being tested for in a variety of formats.** Providers should consider the guidance produced by the Human Genetics Commission on the information that should be provided to potential consumers by companies offering genetic testing. **The Committee of Advertising Practice should more closely monitor the marketing activities of NIPT manufacturers and private hospitals and clinics to ensure that they are not misleading, harmful or offensive. Certification from recognised information quality schemes, such as NHS England's Health Information Standard, should be sought by NIPT providers to help women and couples to know that their information has been quality checked.** Those providing advice to women and couples about privately available NIPT, such as NHS health and social care professionals, the UKNSC and Antenatal Results and Choices, should recommend that women and couples only use NIPT providers that have signed up to such a scheme and have been certified to display its quality mark on their materials.
- 6.40 In addition, to help ensure that women and couples are making informed decisions about NIPT and to reduce the need for women to seek follow-up support and services from the NHS after accessing NIPT in the private sector, **private hospitals and clinics should only offer NIPT as part of an inclusive package of care that should include, at a minimum, pre- and post-test counselling and follow-up invasive diagnostic testing if required.** This should be enforced by regulatory bodies for hospitals and clinics in Scotland, Wales and Northern Ireland, and by the CQC in England when NIPT is within

³⁷⁶ Skirton H, Goldsmith L, Jackson L, Lewis C and Chitty L (2014) Offering prenatal diagnostic tests: European guidelines for clinical practice *European Journal of Human Genetics* **22**: 580-6.

its scope (i.e. when the test is carried out as part of the planning or delivery of an individual's treatment or care). In addition, NIPT should be included in the 'regulated activities' that are regulated by the CQC, to ensure that the provision of NIPT by hospitals and clinics in England is carried out to high standards of quality and safety, even when it is accessed by pregnant women and couples on a one-off basis. **The Working Group does not support the provision of NIPT on a direct-to-consumer basis if these services are not available as part of the package.**

Appendix: Method of working

The Nuffield Council on Bioethics set up a Working Group in April 2016 to explore the ethical implications of recent and potential future scientific developments in NIPT. The Working Group met four times between April 2016 and January 2017. A range of evidence gathering activities, including reviews of research relevant to NIPT and consultation with people with a range of professional and personal interests in NIPT, were conducted between April and December 2016 to inform the deliberations of the group.

Call for views and evidence: anonymous online survey

The Working Group created an anonymous online survey on issues raised by NIPT via the Survey Monkey website, which was open between 19 May and 1 August 2016. The aim of the survey was to gather views from a wide range of individuals, particularly those with personal and professional experiences of prenatal testing and genetic conditions. Survey respondents were self-selecting and the results are not intended to be representative of the views of the population as a whole. In total, 722 people responded to the survey. The Working Group considered an analysis of the survey responses at its second meeting on 23 September 2016. Comments from some of the survey respondents who consented to being quoted are used in this report but the survey analysis will not be published separately in order to respect the confidentiality of respondents.

Survey respondents categorised themselves as follows:

	Response (per cent)	No. of responses
I or my partner has had non-invasive prenatal testing	14	100
I or my partner has recently been or is pregnant	17	121
I am a healthcare professional involved in offering prenatal testing	28	195
I carry out research on or relevant to prenatal testing	5	33
I have another kind of professional interest in prenatal testing	10	68
I have a genetic condition	3	22
A member of my family or a close friend has a genetic condition	47	335
I have a general interest in prenatal testing	14	101
I don't have a particular interest	2	14
Other	15	106
Answered question	98	710
Skipped question	2	12

Survey questions

1. What benefits or concerns do you think offering NIPT as part of NHS antenatal care might raise for pregnant women and their partners?
2. What do you think might be the implications of offering NIPT as part of NHS antenatal care for the healthcare professionals involved in providing prenatal screening?
3. Do you have personal or professional experience of the information and/or counselling currently provided by the NHS to pregnant women and their partners to help them make decisions about currently available prenatal screening (e.g. using ultrasound) for genetic conditions during pregnancy?
4. If yes, how would you rate that information and/or counselling?
5. Do you have personal or professional experience of the NHS providing information or counselling about NIPT available as part of research studies or through the private sector?
6. If yes, how would you rate that information and/or counselling?
7. Do you have personal or professional experience of the information and/or counselling currently provided by private healthcare clinics to pregnant women and their partners to help them make decisions about NIPT?
8. If yes, how would you rate that information and/or counselling?
9. Broadly what information about NIPT and the conditions being tested for do you think should be conveyed to pregnant women and their partners?
10. How do you think that information could best be conveyed, and by whom?
11. Potential parents can find out the sex of their unborn baby for non-medical reasons from ten weeks of pregnancy using NIPT. Do you think this should be allowed?
12. Do you think parents should be allowed to find out the following genetic information about their unborn baby using NIPT in the future?
 - a Information relating to conditions where all babies die before birth or shortly afterwards and for which there is no treatment
 - b Information relating to serious conditions that will affect the child from early in life, for which there is no effective treatment
 - c Information relating to serious conditions that will affect the person in adulthood, for which there is no effective treatment
 - d Information relating to serious conditions that will affect the person in adulthood, for which there is effective treatment
 - e Information relating to less serious health conditions, for which there is no effective treatment
 - f Information relating to less serious health conditions, for which there is effective treatment

g Information about the physical appearance or characteristics of the future child that is not related to a health condition

13. Do you think whole genome sequencing of unborn babies using NIPT should be allowed in future?
14. What, if anything, might the increasing availability and use of NIPT mean for people living with genetic conditions and disabilities?
15. Please use this space to tell us anything else you would like to raise in relation to NIPT.

Call for views and evidence: consultation document

Alongside the survey, the Working Group published a consultation document with a longer series of more detailed questions. The aim of the consultation document was to gather views from organisations and from people whose work focuses on the ethical issues raised by NIPT, such as academics and professionals working in the field. The consultation was open between 19 May and 1 August 2016, and 28 responses were received. The respondents are listed below. The Working Group considered an analysis of the consultation responses at its third meeting on 24 November 2016 and this will be published separately on the Nuffield Council on Bioethics website.

Organisations

Anscombe Bioethics Centre
Association of Genetic Nurses and Counsellors
BioCentre
British Maternal and Fetal Medicine Society
British Medical Association
British Pregnancy Advisory Service (BPAS)
Christian Action Research and Education (CARE)
Christian Medical Fellowship
Church of England, Mission and Public Affairs Council
Clinical Genetics and Cytogenetics, Guy's Hospital
Down's Syndrome Association
Down Syndrome Research Foundation UK
Jane Fisher, Director, Antenatal Results and Choices (ARC)
Genetic Alliance UK
PHG Foundation
Royal College of Obstetricians and Gynaecologists (RCOG)
Saving Down Syndrome
The Liminal Spaces Project, University of Edinburgh, funded by the Wellcome Trust
WeLDNurses
Victoria Woodham, on behalf of Future of Down's

Individuals

Dr Felicity Boardman, Warwick Medical School
Anindita Doig
Matthew Jolly, National Clinical Director for The Maternity Review and Women's Health, Acute Medical Directorate, NHS England
Colette Lloyd

Kay Sammon
Rachel Siden
Lorna Watson

Consultation questions

1. If [the UK National Screening Committee recommendation that NIPT for Down's syndrome, Patau's syndrome and Edward's syndrome be offered on the NHS to pregnant women whose babies are found to have a high risk of having one of these conditions following the 11-14 week screening test] was implemented fully into NHS antenatal care, what benefits or concerns might this raise for pregnant women and their partners?
2. If this recommendation was implemented fully into NHS antenatal care, what might be the implications for the healthcare professionals involved in offering and providing prenatal screening and testing?
3. If this recommendation was implemented fully into NHS antenatal care, it might lead to an increase in the number of terminations of pregnancies with a diagnosis of Down's syndrome, Patau's syndrome or Edwards' syndrome. What benefits or concerns might this raise?
4. Do you think the UK National Screening Committee's criteria for appraising the viability, effectiveness and appropriateness of a screening programme are appropriate for appraising prenatal screening programmes?
5. How would you rate the information and counselling currently provided by the NHS to pregnant women and their partners to help them make decisions about currently available prenatal screening (e.g. using ultrasound) for genetic conditions during pregnancy, if you have experience or evidence relating to this?
6. How would you rate information and/or counselling provided by the NHS about NIPT available as part of research studies or through the private sector, if you have experience or evidence relating to this?
7. How would you rate the information and/or counselling currently provided by private healthcare clinics to pregnant women and their partners to help them make decisions about NIPT, if you have experience or evidence relating to this?
8. What information about NIPT and the conditions being tested for do you think should be conveyed to pregnant women and their partners? How do you think that information could best be conveyed and by whom?
9. What might be the implications for the NHS of increasing numbers of pregnant women purchasing NIPT through the private sector?
10. What benefits and concerns might be raised if pregnant women were able to purchase NIPT directly from providers (e.g. where a kit is sent to the pregnant woman in the post), rather than through a healthcare clinic following a face-to-face consultation?
11. A small proportion of NIPT tests will return an inconclusive result, even if repeated. How should healthcare professionals, both in the NHS and in private clinics, deal with inconclusive results?

12. What issues are raised by incidental findings that can arise following NIPT (such as genetic abnormalities or cancerous cells in the pregnant woman), both in the NHS and in private clinics?
13. Should potential parents be able to find out the sex of their unborn baby for non-medical reasons from 10 weeks of pregnancy using NIPT? Please give reasons for your answer.
14. What genetic information, if any, do you think parents should be allowed to find out about their unborn baby using NIPT? Please give reasons for your answer.
15. What genetic information, if any, do you think parents should not be allowed to find out about their unborn baby using NIPT? Please give reasons for your answer.
16. Do you think whole genome sequencing of unborn babies using NIPT should be allowed? Please give reasons for your answer.
17. What, if anything, might the increasing availability and use of NIPT mean for people living with genetic conditions? Please provide evidence or examples if possible
18. Is current regulation covering the provision and marketing of NIPT in the UK sufficient and appropriate?
19. What ethical values do you think are important or relevant in the context of NIPT?
20. Please tell us anything else you would like to raise in relation to NIPT.

Stakeholder meetings

Three group meetings were held with people with professional and personal interests in NIPT in June and July 2016 to discuss the issues raised by current and potential future uses of NIPT.

Meeting with healthcare professionals involved in the delivery of NIPT, 23 June 2016, London

Attendees:

- Sally Boxall, Consultant Nurse in Prenatal Diagnosis, Princess Anne Hospital, University Hospital Southampton
- Lyn Chitty, Professor of Genetics and Fetal Medicine, Institute of Child Health, University College London
- Rebecca Daley, Senior Clinical Research Midwife, University College London Hospital
- Athalie Melville, Principal Genetic Counsellor, Wessex Clinical Genetics Service and Association of Genetic Nurses and Counsellors
- Dean Meredith, Ultrasound Manager, The Portland Hospital for Women and Children
- Alison Millman, Antenatal and Newborn Screening Co-ordinator, Princess Anne Hospital, University Hospital Southampton
- Ruth Newbury-Ecob, Consultant Geneticist and Honorary Professor, University of Bristol
- Kate Richardson, Lead Sonographer, The Birth Company
- Dagmar Tapon, Genetic Counsellor, Queen Charlotte's and Chelsea Hospital, Imperial College Foundation Trust
- Basky Thilaganathan, Director, Fetal Medicine Unit, Directorate of Children and Women's Services, St George's University Hospitals NHS Trust

Meeting with charities representing people with genetic conditions and people with family members with genetic conditions, 29 June 2016, London

Attendees:

- Kirsty Bassett, Charity Development Manager, Support Organisation for Trisomy 13/18 (SOFT UK)
- Henny Beaumont, mother of person with Down Syndrome and author of *A Hole in the Heart*
- Felicity Boardman, Associate, Spinal Muscular Atrophy Support UK
- Carol Boys, Chief Executive, Down's Syndrome Association
- Elizabeth Corcoran, Chair, Down Syndrome Research Foundation UK
- Penny Green, Director, Down's Heart Group
- Gina Johnston (on behalf of Jayne Hughes), representative of Amy and Friends Cockayne Syndrome Support
- Karen Laudrum, member of Rare Dementia Support Group
- Kerry Leeson-Beevers, National Development Manager and Project Lead for Breaking Down Barriers, Alstrom Syndrome UK
- Andy Merriman, father of person with Down's Syndrome
- Lynn Murray, representative of Saving Downs
- Arti Patel, Information Officer, Understanding Chromosome Disorders (UNIQUE)
- Sally Phillips, broadcaster and parent of child with Down's Syndrome
- Pandora Summerfield, Chief Executive, Down's Syndrome Scotland

Meeting with government, regulatory and professional bodies 6 July 2016, London

Attendees:

- Hilary Angwin, UK National Screening Committee Sub-Committee on Fetal, Maternal and Child Health and Screening and Immunisation Lead, NHS England
- Mark Bale, Deputy Director, Genomics, Science & Emerging Therapies, Department of Health
- Sarah Bower, Consultant in Fetal Medicine, British Society for Maternal and Fetal Medicine
- Natasha Dare, Policy Manager, Nursing and Midwifery Council
- Martin Davies, Senior Policy Adviser, British Medical Association
- Sadaf Ghaem-Maghami, Royal College of Obstetricians and Gynaecologists
- Jenny Hewison, Professor of the Psychology of Healthcare, Leeds Institute of Health Sciences
- Stephen Lee, Biosciences Team Manager Devices Division, Medicines and Healthcare products Regulatory Agency
- Anne Mackie, Director of Programmes, UK National Screening Committee
- Rona McCandlish, Guidelines and Audit Adviser, Education, Royal College of Midwives
- Robert Morrison, Senior Regulatory Policy Executive, Committee of Advertising Practice
- Vibha Sharma, Policy Officer, Standards, Ethics and Education Policy, General Medical Council

Other meetings

A meeting with Jane Fisher, Director of Antenatal Results and Choices was held on 6 July 2016.

A meeting with Victoria Woodham of Future of Down's was held on 3 August 2016.

Interviews with scientists working in areas relevant to NIPT

Interviews were conducted in July and August 2016 with scientists working in relevant fields, including in the analysis of cell free DNA, behavioural genetics and prenatal fetal treatments, in order to explore how NIPT might be used in the future.

- Diana Bianchi, Director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), Maryland, United States
- Dennis Lo, Director of the Li Ka Shing Institute of Health Sciences, Professor of Medicine and Professor of Chemical Pathology, The Chinese University of Hong Kong
- Robert Plomin, Professor of Behavioural Genetics, King's College London
- Anita Thapar, Clinical Professor, Division of Psychological Medicine and Clinical Neurosciences, Cardiff University

Interviews with manufacturers of NIPT

The manufacture and provision of NIPT and possible future developments in NIPT were discussed with representatives of three NIPT manufacturers in July and August 2016.

- Representatives of Illumina
- Xiaofan Zeng, Director of Science and Technology Office, BGI Shenzhen
- Stephen Little, Chief Executive Officer, Premaitha Health

Interviews with women who had recently undergone NIPT

One-to-one interviews were conducted with three women who had recently undergone NIPT in which they discussed their own experiences and views. The interviews were conducted by members of the Working Group with counselling experience and took place in October 2016.

Interviews with people with genetic conditions

Interviews were conducted with people with a genetic condition or impairment to explore their experiences and personal perspectives on the issues raised by NIPT.

Between August 2016 and January 2017, the Working Group collaborated with the national learning disability charity Mencap to carry out interviews with people with Down's syndrome. Dr Barbara Barter, Clinical Psychologist, was recruited to lead the consultation exercise and carry out the interviews. The interviews were preceded by a recruitment process to identify suitable participants carried out with the support of advocacy and campaigning organisations across England. People who were interested in taking part were invited to attend information sessions covering related topics, including sex and relationships, difference and diversity and prenatal screening and termination. Interviews with six people with Down's syndrome were included in the consultation exercise. A detailed report by Dr Barbara Barter outlining the method and findings of this work has been published separately, at: www.nuffieldbioethics.org/NIPT

Further interviews were carried out with three people with other genetic conditions which NIPT can be used to test for. The interviews were conducted in November and December 2016 by members of the Working Group with counselling experience. One interviewee had spinal muscular atrophy, one had cystic fibrosis and one was a carrier of a balanced translocation genetic variation and had a child with Emanuel syndrome.

Evidence reviews

The Working Group commissioned a review of literature and evidence on the factors affecting decision making by pregnant women and couples about prenatal genetic screening and NIPT. Dr Gareth Thomas, Lecturer in Sociology School of Social Sciences Cardiff University carried out the review and it has been published separately at www.nuffieldbioethics.org/NIPT.

In-house reviews of research on the impacts of prenatal screening on disabled people; laws and regulations relevant to NIPT; and patient information provided to women and couples seeking NIPT were also carried out.

External review

A draft version of the report was circulated in December 2016 to six external reviewers with professional expertise of one or more issues connected to NIPT. Reviewers' comments were considered at the Working Group's final meeting on 23 January 2017.

The reviewers were:

- Owen Barr, Professor of Nursing and Head of School of Nursing, University of Ulster
- Roger Brownsword, Professor in Law, King's College London and Bournemouth University
- Jenny Hewison, Professor of the Psychology of Healthcare, Leeds Institute of Health Sciences
- Dennis Lo, Director of the Li Ka Shing Institute of Health Sciences, Professor of Medicine and Professor of Chemical Pathology, The Chinese University of Hong Kong
- Pranav Pandya, Director and Clinical Lead for Fetal Medicine services, University College London Hospital
- Stephen Wilkinson, Department of Politics, Philosophy and Religion, Lancaster University

How the evidence is referred to in the report

In this report, we have used quotes from people with whom we have engaged during the project, where permission for this has been given, in order to illustrate how issues raised by NIPT are experienced by different people. We refer to those with whom we have engaged as follows:

Survey respondents

- Person with experience of undergoing NIPT – survey respondent
- Person with recent experience of being pregnant – survey respondent
- Healthcare professional – survey respondent
- Researcher – survey respondent
- Person with a general professional interest in prenatal testing – survey respondent
- Person with a genetic condition – survey respondent
- Person with a family member or close friend with a genetic condition – survey respondent
- Person with a general interest in NIPT – survey respondent
- Person with no particular interest in NIPT – survey respondent

Interviewees

- Woman with experience of undergoing NIPT – interviewee
- Person with a genetic condition – interviewee
- Carrier of a genetic condition – interviewee

- Person with Down's syndrome – interviewee

Consultation respondents

- Named organisation or person – consultation respondent
- Anonymous organisation or person – consultation respondent